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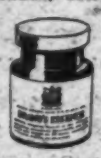

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY MARCH 10 1951

THE HUNTERIAN HERITAGE*

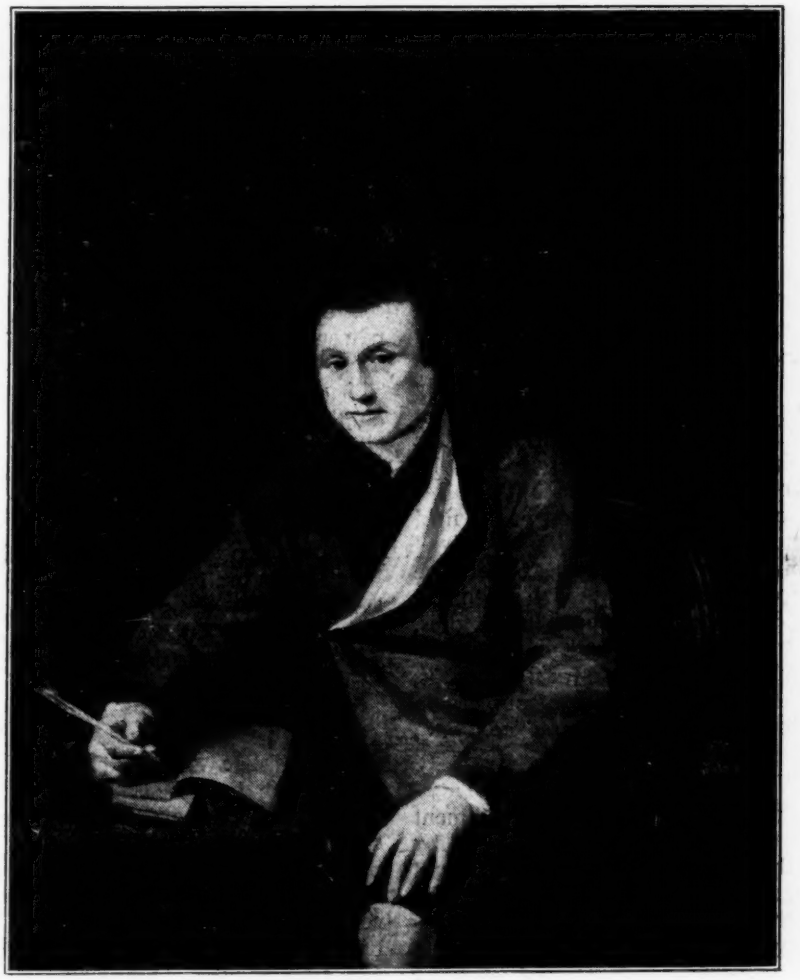
BY

Sir MAX PAGE, K.B.E., C.B., M.S., F.R.C.S.

Consulting Surgeon, St. Thomas's Hospital

John Hunter was born 222 years ago and died in October of 1793, on the same day that Marie Antoinette was guillotined in Paris.

To-day we once again commemorate his life and work. When one considers how little direct evidence of his influence on modern surgery can be traced we may wonder if there is not something of myth in our current conception of him. Yet, though standards vary, the core of greatness remains, and it may be said that it is the true mark of genius that it can survive changing standards. Hunter was great to his contemporaries, and when we contemplate his achievements he remains great to us after the passage of nearly two centuries.



John Hunter. By Home.

The circumstances of John Hunter's early life and his introduction to London by his brother William are, I know, familiar to many of you, but by no means to all, and I think it is worth while considering once again what manner of man he was, what was his education, and the matter and method of his work, and thereby trace his influence on modern surgery.

He was the tenth child of a small Lanarkshire laird who was 68 when John was born—an interesting fact for the geneticists. His mother, 20 years younger, was the daughter of a successful Glasgow maltster, and upon her fell the main responsibility for John's upbringing, as her husband died when John was 13 years old.

He was sent to school at Kilbride, but seems to have been little disciplined there or in the home. According to the available evidence John was no great help to his mother, and was, moreover, a poor scholar, or, at any rate, an unwilling one. Anne Baillie wrote that "he would do nothing but what he liked, and neither liked to be taught reading and writing, nor any kind of learning, but rambling among the woods and braes. . . ." He himself remarked in later life that, "when a boy, I wanted to know all about the clouds and grasses and why the leaves changed colour in the autumn; I watched the ants, bees, birds, tadpoles, and caddisworms; I pestered people with questions about what nobody knew or cared about."

His early education was certainly defective, but in 1755, presumably on the instigation of his brother, he was sent up to St. Mary's Hall, Oxford—now incorporated with Oriel. It would appear that he spent only one term there and that education in the classics in no way suited his genius, for he said later to Sir Anthony Carlisle, "They wanted to make an old woman of me; or that I should stuff Latin and Greek at the University—these schemes I cracked like so many vermin as they came before me." It is quite clear that the Latin school of Kilbride

*The Hunterian Oration, delivered at the Royal College of Surgeons of England on February 14, 1951.

and Oxford of that day had little to offer such a determined naturalist. Verbal felicity and a happy command of language were not among Hunter's attributes. Though inherent in a few, they are characteristics best developed by the system of teaching at our older universities. Of great value in almost any field, they are not necessary to the successful man of action, and I think that John Hunter comes into that category.

An Important Influence

At the age of 17 he was sent to live in Glasgow with his married sister, Jane. Her husband was a timber-merchant and cabinet-maker, and John probably took his share in the activities of the workshop. It clearly did not satisfy him as a career, and when he was 20 (1748) he rode up to London on the invitation of his brother William, who at that time was firmly established as a physician and teacher of anatomy. Sampson Handley in 1939 gave an attractive account of the latter's career and of his teachers, the Douglases. Sampson Handley considers that the influence of this little group of London Scotsmen was of the greatest importance in the development of John's special abilities. For eight years he lived with his brother in Covent Garden and worked steadily at anatomy, and undoubtedly this was the important educational period in his life. He proved most efficient at his work in the dissecting-room, and made, or helped his brother to make, original discoveries in the placental circulation and on the method of descent of the testis. As dissection in those times was possible only in the winter months, he had much time to spare. Speculations on how he filled it have afforded free play to his biographers. In the century of enlightenment London was certainly an attractive place for a young man, but no reliable facts are recorded of his diversions. By way of study it is known that he attended some hospital teaching in 1749 and 1750 at the Chelsea Hospital, working under Cheselden, who was then just due to retire. In 1753 he was elected Master of Anatomy at Surgeons' Hall—clear evidence of his outstanding distinction in the field of his work up to date. It may be noted that Percivall Pott, though much his senior, was elected at the same time. After the Oxford interlude in 1755 he returned to London, attending St. George's Hospital for lectures, and was appointed house-surgeon to that institution in 1756. This resident appointment he held for five months, and it formed his only close experience of surgery in civil life before he embarked on private practice.

On Active Service

An important break in routine was his appointment in 1760 as a staff surgeon to the Army. It was said by Home that he joined the Army for reasons of health and that he had at that time the threatenings of consumption. It seems more likely that to a man of his energetic temperament the change was inspired by boredom with life in London coupled with a desire to travel and see more of the world. Moreover, it is difficult to believe that even in the eighteenth century a man would embark on active service for the cure of a chest complaint. It may be noted that in his letters to his brother from the Army the matter of his health is never mentioned—postings and pay, as was usual in the days of patronage, being the major issue.

He was appointed to the force destined for the attack on Belle Isle towards the end of the Seven Years War. Robin Adair was Inspector-General of Hospitals about this time, and, being acquainted with the Hunters, he is presumed to have been responsible for the appointment. The operation was an amphibious one, and most of the wounded men were taken back to the ships for treatment after the two actions, the second of which was successful. In this interlude Hunter gained his experience of war surgery, and in his last work he quotes examples of the primary healing of wounds then observed. In his spare time he also pursued his bent for natural history and dissected eels and other fish. He also dates the draft plan for his work on the blood and inflammation to this period.

In 1762 he was transferred to Lord Loudoun's force in Portugal, being posted as surgeon to a hospital commanded by one William Young. John's letters to his brother during this service give some glimpses of the course of events and his own reaction to them. Of his two chiefs in the hospital he said, "They were as unfit for their jobs as the Devil to reign in heaven"; and, further, "God help the hospital when directed by such two." He was also concerned to augment his salary, which was 10s. a day, and put in a plea that he should be appointed deputy director of the hospital and on another occasion deputy purveyor. In a later letter from Portalegra dated November 11, 1762, he says he is applying for the post of physician—"If I get that I shall be a Doctor as well as the best of you. I have attended his Lordship in all his marches, and have reason to believe I am well with him."

One may conclude that at this time, when he was 34, he was by no means confirmed in his own estimation as a surgeon, and indeed showed a very simple, human, and opportunist ambition quite natural in an age when patronage was so often the key to advancement in life.

The campaign in Portugal did not result in much fighting, and the hospital problem was mainly one of accommodation and evacuating the large number of sick. The late lamented George Gask wrote an admirable account, based on the Loudoun letters, of the hospital organization and Hunter's relations with it during this campaign. While in Portugal it would seem that Hunter was pretty fully employed in medical and minor administrative duties: his only written reference to scientific observations appeared in his paper, "An Account of the Hearing Organ of Fishes," which was not read till 1782.

Practice in Golden Square

An armistice was signed at the end of 1762 and Hunter returned to London in May, 1763. He then went on half-pay and set up as a practising surgeon in Golden Square. Foot says he opened a room for dissections, but how far this was with the object of teaching or for research is not known. His work and his strong personality must, however, have attracted notice, for in 1767 he was elected a Fellow of the Royal Society and in 1768 appointed surgeon at St. George's. His intense interest in the active pursuit of natural history can be dated from this period, for in 1764 he bought two acres of land at Earl's Court and built a cottage and stables on it; here he gradually established an extensive menagerie and experimental farm.

In 1771 he published his book on diseases of the teeth, illustrated by some excellent engravings by Sharp. The anatomical section of this work is admirable and is said to require little alteration to-day. On the clinical side he brings out his enthusiasm for the transplantation

Mrs. John Hunter.

of teeth and devotes much space to the theory and practice of the procedure. In relation to this activity Foot accused him of being mainly concerned with arousing the attention of dentists and gaining their patronage. Certainly the practice excited much public interest, evidence of which is shown by Rowlandson's cartoon on the subject. It must be said that Hunter, in his convictions on the value of hetero-transplantation, seems to have been unduly influenced by the outstanding successes and was slow to detect the drawbacks and dangers of the procedure. With the improvement in prosthetic dentistry the practice gradually died out except for a remarkable revival staged by Valadier during the 1914–18 war.

In 1771 he married Anne Home, sister of one of his pupils, and went to live in Jermyn Street. His wife was an attractive and gifted woman. She bore him four children, two of whom survived him. Her gift for light verse, her musical interests and social leanings, were in sharp contrast to her husband's scientific and almost asocial concentration, but, despite their divergent interests, she seems to have lived on good terms with him until his death. Hunter's life for the next 20 years continued in London, and, except for visits to Bath and Tonbridge for health reasons, he did not leave it. If we are to believe Ottley (1835), who quotes the faithful Clift, his daily routine was to start work at 5 or 6 a.m. After dinner, at 4 p.m., he took an hour's sleep; then worked till 1 or 2 a.m., and slept for only some four hours.

Experimental Work

The amount of work Hunter got through was certainly prodigious. At his death he had collected and made or dictated notes on 8,000 specimens. Owen, in editing Hunter's *Animal Oeconomy*, states that he anatomized at least 500 species of animals, exclusive of repeated dissections of different individuals of the same species, besides the dissection of plants to a considerable extent. He was progressively more sought after in consultation as a surgeon, and yet had time after 1785 to organize his museum in Leicester Square and, in some degree, control his employées, whom Clift estimated never to number less than 50. He continued up to the end to conduct experiments and dissect specimens at his farm at Earl's Court as occasion arose. Hunter's correspondence with Jenner, of which a good deal has survived, gives an impression of his activities and interest in this field. He was willing to give commonsense advice on surgical problems, but his main theme was always natural history and repeated demands for specimens. The following are some revealing examples:

January 10, 1776.

"DEAR JENNER,

"You must think me very fond of fish when you sent me cheese as much fishified as possible; however, it is an excellent cheese. . . . I have but one order to send you, which is, to send everything you can get, either animal or vegetable, or mineral and the compound of the two, either animal or vegetable mineralized. I would have you do nothing with the boy but dress him superficially; these funguses will die, and be damned to them, and drop off. Have you large trees of different kinds you can make free with? If you have, I will put you on a set of experiments with regard to the heat of vegetables. Have you any eaves where bats go at night? If you have, I will put you upon a set of experiments concerning the heat of them at different seasons.

Ever yours,
J. H."

On January 22 following, the brain fungus is again referred to:

". . . if it is brain let it drop off; if it is fungus let it either drop or waste off. Therefore be quiet and think yourself well off that the boy is not dead. . . . You do not mention

Teeth transplantation. By Rowlandson.

a word about bats. . . . Have you got the bones yet of a large porpoise? I wish you had. Is ever the salmon spawn seen after she has parted with it? If it is, I wish you could get some: I want to examine the spawn of fish in the progress of the formation of the young one.

Yr. most obedient servant,

J. H."

Surgery at St. George's

In 1775 he began systematic lectures on surgery at St. George's. The course consisted of 86 lectures, which were read. By all accounts his delivery was poor; the subject matter dealt more with principles than with practice, and attendances were not good. Yet his more able pupils or disciples, such as Home, Cline, Astley Cooper, Lawrence, and Abernethy, valued them highly. His appointment in 1776 as Surgeon Extraordinary to the King is evidence of his established reputation in practice.

In 1780 his conflict with his brother William on the authorship of a discovery in relation to the placental circulation came to a head. They were both hot-tempered and obstinate in such matters, and the quarrel had not been made up when William died in 1783. It was in that year that he bought a 24-years' lease of premises in Leicester Square and expended £3,000 on building a museum and lecture theatre; the project was completed in 1785, and his collection was assembled there by Bell and Clift.

At this time Mrs. Hunter reports him as tormented with the "flying gout," and he went out of town for six weeks for a cure. He seems to have returned in fair health, for in December he carried out his first operation of distal ligature for popliteal aneurysm. Details of this innovation and arguments in favour of it were published after Hunter's death by Home, eight cases in all being quoted, with three deaths. It is interesting to note that until 1785 Hunter had considered the direct approach to be the correct one. Suppuration followed by secondary haemorrhage, however, was so common after this procedure that the English surgeons of that day advised primary amputation as the proper course for popliteal aneurysm if radical treatment became imperative. It may be remarked that even when the distal operation was generally adopted some suppuration about the ligature always took place and that serious secondary haemorrhage remained a common complication.

Hunter's Writings

Hunter's treatise on venereal disease was published in 1786, and French and German translations appeared shortly afterwards. This book forms a landmark in the scientific approach to the subject, the knowledge of which till then had been chaotic and the treatment too often left in the hands of quacks. It is noticeable, however, that Hunter's conclusions did not greatly advance the treatment of the conditions he investigated: he distinguished hard and soft chancre, but held firmly to the opinion that syphilis and gonorrhoea were caused by the same virus—an opinion strengthened by the experimental inoculation he carried out on himself. His advocacy of the caustic treatment of strictures did not remain in vogue for long, and one can guess that it was followed by many recurrences of the primary trouble.

His major work, *Treatise on the Blood, Inflammation, and Gunshot Wounds*, was not published till just after his death. It does not make easy reading, and revision would no doubt have eliminated many of the repetitions. It is tinctured with the metaphysical physiology of the period, and the author discusses at length "sympathy" in the body, subdividing it into three types. He recognized the existence of the red globules, but was sceptical of the detailed description of the blood by Leeuwenhoek and Morgagni, for he says: "These early observers imagined more than they saw." It is noticeable in all his work that in the main he trusted to naked-eye appearances. At most he seems to have used a magnifying glass, although Hooke had completed his compound microscope almost a century earlier. Of inflammation, though systematic, he does not make a very clear picture, which is not surprising considering the poverty of his means for observation: the terms he employed to illustrate his views were new to his contemporaries and do not convey a clear meaning to us to-day. In all his writing, reference to his predecessors' work is seldom in evidence and no acknowledgment of sources is made—to a degree which is surprising to us. However, it had the merit of revealing his independence of authority and his originality in thought. The results of his dissections and observations on the lower animals were mostly left in his note-books, but under the title *Animal Oeconomy* a group of papers on disconnected subjects was published in one volume in 1786. His contributions to the study of comparative anatomy were amplified by Richard Owen, who, from the surviving notes, brought the number of papers up to 48 in his 1835 edition. Interesting as evidence of his industry and curiosity though these various publications are, to-day it is his museum, with its additions and losses, that remains the principal monument of his life. Professor Grey Turner a few years ago devoted a learned and interesting Oration to its birth and development, and in so doing paid one of the outstanding tributes to Hunter's memory.

The circumstances of Hunter's death after an altercation in committee at St. George's are familiar. From the post-mortem appearance of his coronary arteries and aorta it is evident that his hold on life can have been but precarious for some time before his death. Hunter was himself conscious of this, and had said several years back that his life was in the hands of any rascal who chose to provoke him.

Assessment of His Work

In attempting to get a true picture of this remarkable man one realizes how difficult it is to reconstruct the past. It may be simpler to inquire into the views of successive generations of surgeons on his character and ability, and so perhaps trace the gradation from admiration modified by lack of comprehension or jealousy to the more balanced appraisal of his merit which developed in the lapse of time. Hunter's brother-in-law, Everard Home, in virtue of having been first a pupil and later his trusted assistant, was best qualified among his contemporaries to know his work most accurately and to assess it most justly. The fact that Home subsequently pirated much of Hunter's notes and then destroyed the evidence does not, I think, militate against his evidence on an earlier period.

Home's short and somewhat abrupt account of Hunter's life was appended in 1794 to the first edition of *The Blood and Inflammation*. In places it bears evidence of a feeling of annoyance and disappointment that at his death Hunter had left so little provision for his wife and family. The following quotations give the

core of his observations: "In the practice of surgery, where such cases occurred in which the operations proved inadequate, he always investigated with uncommon attention the causes of that want of success." "I had now lived six years with Mr. Hunter, and had completed my education. His expenses had always exceeded his income; I had therefore no emolument to expect from remaining in his house." And so Home went off to the West Indies as a naval surgeon, returning six years later to become Hunter's assistant. Later Home says, "Such was his turn for investigation and so extensive the scale upon which he instituted inquiries, that he always found something more to be accomplished"; and, "He was always solicitous for some improvement in medical education"; and in 1787, "His collection, which had been the object of his life . . . was now brought into a state of arrangement." "The collection of comparative anatomy which Mr. Hunter has left . . . must be allowed to be a proof of talents, assiduity, and labour which cannot be contemplated without surprise and admiration."

Portrait bust of Sir Everard Home.

Personal Characteristics

Of Hunter's personal qualities Home says: "His temper was very warm, impatient, readily provoked, and when irritated not easily soothed. His disposition was candid and free from reserve, even to a fault. He hated deceit and he was above every kind of artifice; he detested it in others and too openly avowed his sentiments." "In conversation he spoke too freely and sometimes harshly of contemporaries." "Public-spirited to an extreme, he valued money no further than as it enabled him to prosecute and extend his various and nearly universal researches. . . . He paid too little attention to his own and his family's interest."

Of his practice he records that Hunter's income was never over £1,000 a year till 1774, but that it rose to £5,000 several years before his death, and lastly to above £6,000. "In private practice he was liberal, scrupulously honest in saying what was really his opinion of the case, and ready when occasions arose to acknowledge his ignorance whenever there was anything he did not understand."

Another contemporary biographer, Jessé Foot, whose main claim to respectability was based on his having held the post of house-surgeon at the Middlesex Hospital, broke into print early in 1794. He was so much concerned with decrying Hunter's work and belittling his motives that his testimony is of little value. Jealous spite must surely have inspired such a statement as, "I am authorized to pronounce him, to have been, a very inferior, dangerous and irregular practical surgeon." On the other hand, he recognized Hunter as "one of the most industrious of men," and, in extenuation of his quarrels with his fellow surgeons at St. George's, mentions the poor health which dogged him in his later years. Some idea of Foot's pretentious style of writing may be gauged from his method of expressing this: "The palpable diseased irritation of his mind, exacts all the apology, which humanity founded upon reason can bestow."

Foot's description of Hunter's physical appearance is probably reliable, and is as follows. "His person was about the middle stature: he was rather robust but not corpulent: his shoulders were broad and high, and his neck remarkably short: his features were hard,—cheeks high—eyes small and light—eye lashes yellow, and the bony arch protruded. His mouth was underhung." Dr. Beddoes, a versatile contemporary physician best known on account of his association with Lavoisier, Davy, and Priestley and for his therapeutic use of gases, makes the following notes on Hunter: "He fancied what he could not find words for, very profound. But he was mistaken. Whenever he found himself at a loss for words he was labouring with the delivery of nonsense." But he also writes: "When one heard of John Hunter as the first surgeon in London one felt a pleasure like that which arises from the distribution of poetical justice."

In the recently published *Diary of Sylas Neville* (1950) there are references to Hunter which throw some light on his contemporary reputation outside London. Neville, born in 1741, was a man of mysterious ancestry, small private means, and strong Whiggish sympathies. Dissatisfied with the life of a small Norfolk squire, he decided in 1771 to try medicine. He also had the intention thereby of augmenting his somewhat precarious income. In this he does not seem to have been successful, perhaps on account of a temperament of artistic sensibility coupled with a hesitating and anxious attitude towards life. His diary covers the years 1767–88. The first entry I shall quote appears in October, 1771, when Dr. Manning, a Norwich friend, is advising him to go to Edinburgh for his medical studies—"He says Hunter is an ill-natured waspish creature"—so to Edinburgh Neville went and completed his time under Cullen. When he left for London in 1776 Dr. Cullen advised him to take "one course of Hunter, to see his preparations accompanied by his demonstrations." In the entry of October 1, 1776, the entry appears: "Began to attend Dr. Hunter's course on anatomy. He gave his first lecture this day. He is an indifferent-looking little man, so that his figure is rather against him and his theatre is neither so large nor so elegant in any respect as Monro's." Regrettably Neville makes no further entry about his medical studies in London, and seems to have been more interested in the theatre and his own financial and domestic difficulties.

The Immigrant Scot

It is hard to assess the degree to which Hunter in the second half of the eighteenth century was affected by prejudice against the immigrant Scot. One may remember that Culloden preceded the period under consideration only by 20 years and that Scotland was still far from prosperous. Jessé Foot's diatribes and the antagonisms of his colleagues at St. George's are plain evidence of the jealousy aroused in small minds, but the sentiment was by no means limited to such. Dr. Johnson's quips have feeling behind them. We are familiar with his apostrophe: "But, Sir, let me tell you, the noblest prospect which a Scotchman ever sees, is the high road that leads to England." Said Boswell: "I do indeed come from Scotland, but I cannot help it."

To which Johnson replied, "That, Sir, I find is what a very great many of your countrymen cannot help"; and again, "Sir, it is not so much to be lamented that old England is lost as that the Scots have found it."

A counterblast to such sentiments from the other side of the Border may be found in a letter from David Hume, the historian and philosopher, dated from Edinburgh in 1776. He was writing to congratulate Gibbon on the first volume of his *Decline and Fall*, and in it he says: "Such a performance from an Englishman in our age would have given me some surprise. You may smile at this sentiment, but, as it seems to me that your countrymen for almost a whole generation have given themselves up to barbarous and absurd faction, and have totally neglected all polite letters, I no longer expected any valuable production ever to come from them." That some mutual prejudice existed is clear, and perchance such feelings are not yet quite dead.

Contemporary Opinions of Hunter

To continue with the views of his contemporaries, Sir Astley Cooper, one of the outstanding surgeons of the early nineteenth century, and a noble figure of a man, had a great admiration for Hunter, having attended his lectures in 1788. In his own lectures Cooper always refers to Hunter with veneration, although he is critical of some of his methods in surgical practice.

Abernethy, an ornament of Bart's, and one of Hunter's few friends among London surgeons, in his oration of 1819 called Hunter "a shrewd man, aye and a benevolent man too." He spoke of "the zeal with which he assisted every poor man of merit," and said he was humble-minded and a man of very considerable humour.

Sir Anthony Carlisle, another contemporary, in the oration of 1820 dressed his tribute in flowery language. Of him he said: "Reared and cherished in the Metropolis, the genial warmth of its public-minded inhabitants expanded all his energies, and their liberal discrimination supported him through those difficult, laborious, and expensive researches which were consecrated to the advancement of Medical Science." As a counter to this I may quote from Green, surgeon, philosopher, and friend of Coleridge, who in his oration of 1840 observed of Hunter: ". . . who at the sacrifice of fortune and present enjoyment to the cause of science, laboured with undaunted perseverance, amid the sneers of his contemporaries in the execution of his great work."

Edward Jenner was Hunter's favourite pupil and the only scientific friend with whom he regularly corresponded. Ottley (1835) published a number of Hunter's letters, some of which I have already quoted. Unfortunately, Jenner's side of the correspondence has not survived. In his life of Jenner Dr. Baron says: "I was interested to hear Dr. Jenner . . . discoursing on the commanding and engaging peculiarities of Mr. Hunter's mind. He generally called him the 'dear man' and . . . described the honesty and warmth of his heart."

Of contemporary opinion abroad the main evidence we have is Hunter's election to membership of the French Royal Academy of Surgery in 1783 and the fact that all his major publications were translated into French and German within a year or so of their publication in England.

When we pass to opinions of the Victorian period the tone changes. Benjamin Travers in 1838 quoted Dr. Latham as saying, "Pardon me if I hold that Hunter was only nominally a surgeon; he belonged to no isolated district of one profession and he is at this moment rendering aid to the labours of Physicians."

Later Evaluation of Hunter

Sir James Paget in 1877 composed one of the best and most fully documented studies of Hunter's life and work. He analysed the source of his intellectual activity, his power of natural observation, and also his passion as a collector. He said of him: "In all his practical writings we can detect the same scientific mind as was at work in physiology; the same care and laborious activity in collecting facts; the same quickness and usual accuracy in generalizing; but the whole effect is to 'be master of all the facts.'" Paget's conclusion, "Yes! Hunter did more than anyone to make us gentlemen," sounds a note which rings a little oddly to our generation.

Lord Lister admired Hunter and set much store on an annotated copy of Palmer's edition of his works and one of Sharp's engravings of the Reynolds portrait. Godlee in his *Life of Lister* draws a comparison between Hunter and Lister, noting how the first was extraordinarily diffuse in his interests, whereas the latter concentrated his activity, and in the event achieved so much more.

Savory's aphorism on Hunter in 1887 merits quotation: "He affected more by the questions he put than by the answers he worked out."

Later foreign evaluation of Hunter may be estimated from the measure to which his books continued to be translated. Quoting from Mr. LeFanu's full bibliography, one finds there were publications in French and German of his *Venereal Disease* as late as 1859, and of the *Blood, Inflammation, and Gunshot Wounds* in 1892. In a letter to Mr. Holden from Vienna in 1880 the great Billroth opens with the words, "I honour J. H. as one of the greatest men the English nation has hitherto brought forth, and I have often referred to him in my writings."

The substance of the orations of the current century will be more familiar, and I will confine my quotations to a few outstanding examples.

In 1927 Lord Moynihan in one of his polished addresses analysed the work of Lister and Hunter. Of Hunter he says: "There has probably never been a man in one profession with so wide an intellectual interest, so profound a knowledge of so many varied subjects wholly derived from direct personal inquiry and observation. He had no equal either as pathologist or as physiologist; he was already first among comparative anatomists, and was indeed one of the founders of the science." In tracing Hunter's intellectual background he remarked: "William Hunter, who impregnated the mind of his brother, drew his own inspiration and owed his intellectual guidance to the Monro–Cullen school in Edinburgh."

Wilfred Trotter, in 1932, in a characteristically philosophic essay, said: "Hunter was a consistent and expert user of the experimental method in the study of living processes, and it is on this fact that his fame essentially and ultimately rests. Further, it is impossible, however, not to be struck by a certain disproportion between the amount of energy and genius that was expended and the harvest of substantial knowledge that was gathered. Many of the researches were indecisive, not a few of the conclusions were incorrect, and no single advance

was won which could be said to mark an epoch in the history of knowledge."

Trotter attributed this relative failure to the atmosphere of embryonic science of Hunter's time and to the primitive equipment with which he worked on problems which have since only gradually yielded to all the resources of the modern world.

Professor Grey Turner, as I have already mentioned, wrote an outstanding monograph on the museum and its development, a subject to which Sir James Walton also contributed valuable observations. Professor Wood Jones in his new introduction to the museum points out that it may be termed a collection of specimens illustrating the great principles of the interdependence of structure and function.

His Enterprise

An aspect of Hunter's character which has not received much attention was his remarkable enterprise and business ability. This became evident after his return from Portugal in 1763: his aim to devote his main energies to research and experiment in the animal field had by then crystallized. His purchase in the following year of the Earl's Court farm, and his building programme, form the first outstanding move in support of this aim. How he managed it without capital and with the half-pay of a staff surgeon as his only secure source of income remains mysterious and surprising. He was always ready to pay a good price for any unusual specimen of animal life—alive or dead—and his bargain of £500 to the resurrection men for the body of James Byrne, the Irish giant, in 1784 is one of the high spots in this respect. It also illustrates his passion for collecting the abnormal or unusual. Byrne was one of the curiosities of the town, and he is included in one of Rowlandson's cartoons. Sylas Neville went to see him, and makes the following entry in his diary on January 4, 1782: "Saw Byrne, the famous Irish Giant, in whose person Nature has exceeded her usual limits in a most astonishing degree. Even the great Patagonians are nothing to this—8 ft. 2 in. Tall men walk considerably under his arm; but he stoops, is not well shaped, his flesh loose, and his appearance far from wholesome. His voice sounds like thunder, and he is an ill-bred beast, though very young—only in his 22nd year."

Another example of Hunter's independence and enterprise is afforded by his setting up a private printing press in 1786. From this he produced and sold his books direct to the public. The purchase of the lease of the Leicester Square property in 1783 and the consequent ambitious building programme are a further reminder of the big way in which he managed his affairs. Professor Wood Jones thinks it was remarkable that he managed to obtain so many glass specimen jars for his collection at a time when they were not regularly manufactured. His passion as a collector of protean interests is shown by the contents of his museum. At his death it contained, beyond the many preparations pertaining to the animal economy, a large collection of fossils, several suits of armour, weapons, and pictures. At the sale of his effects after his death, pictures and engravings fetched £940, "curiosities" £200, and books £160. How he acquired the Stubbs pictures, which remain in our museum, we do not know. It is unlikely that they were commissions, as it is recorded that Stubbs's recognized fee for the portrait of a racehorse from 1760 onwards was 100 guineas. Hunter admired Stubbs's paintings, and mentions in a letter to Jenner that he had picked up for £5 one of his studies of a lion attacking a horse—perhaps it was a copy.

In my brief sketch I fear I have given but an incomplete picture of Hunter and a bare outline of the results of his impact on the surgeons of his own and later periods. His influence on the practice of surgery, so far as it was immediate, was not great. He was unquestionably the initiator of the scientific approach; but, technically, surgery could make no substantial advance till the advent of anaesthesia followed by asepsis opened wide the door. It was in the sphere of medical education as a whole that his influence bore more immediate fruit.

Present Aims in Surgical Education

To-day, mainly owing to the vision and energy of Lord Webb-Johnson and the munificence of Lord Nuffield, this college is embarked on a full policy of postgraduate education in surgery. With both the examining and the teaching for an essential diploma in its hands the college is now endowed with an almost monopolistic power whereby it can mould English surgery. We shall therefore have to guard against the imposition of a uniform official pattern on our graduates. Our aim should be to secure in our diplomates an inquiring and critical attitude of mind. Gibbon observed that of the two educations a man had—the one given to him and the one he gave himself—the education he gave himself was by far the more important kind. Hunter certainly relied mainly on the latter type. It is not my intention to suggest that in matters educational we can draw dogmatic principles from the example of genius, but one may emphasize the importance of allowing fair play to independent thought and action at all levels.

Our primary examination is founded on the so-called basic sciences. What these exactly should be is in some degree on trial and *sub judice*. Ideally the subject matter should vary in accordance with the course of undergraduate education undergone by the candidate; but to contrive such adaptability is hardly practicable. There is a general agreement that a full knowledge of human anatomy must remain as the foundation of the surgeon's education. With the ever-continuing extension of specialized knowledge in physiology and pathology, the drafting of a reasonable syllabus in these subjects becomes more and more difficult. Some would add, or substitute for items in the current model, elementary logic and some study of the history of philosophy; others have suggested a knowledge of statistical methods. However, whatever the outcome in the introductory phase our final aim is the education of practical surgeons, and with this in view we should not forget that surgery is a craft as well as a science, and that it deals with human bodies and personalities. I think we should bear this ever in mind and take care that lectures do not hold too prominent a place in our system. They help to get the student through examinations, but do not necessarily make him a competent doctor or give him a working knowledge of human relationships. They impart knowledge but cannot give wisdom. The place to develop this is in the hospital, where contacts with the teacher are on a different plane and where a man's own observations can be brought to bear on the problems of the sick, where responsibility is shared, failure can be analysed, and success appraised. In regard to the method of assessment in the final examination, I cannot help thinking that soon we must allow greater credit to

the practical training the candidate has undergone rather than give too much weight to his mastery of multiple facts and divergent opinions.

A Need of To-day

To turn to another facet of the Hunterian heritage—we all probably accept the truth of Lawrence's aphorism, "Thus we find at last the difference between physic and surgery is a distinction not in science but in practice." Mr. Victor Bonney in his eloquent oration of 1942 made out a strong case for some integration of the many specialties into which medicine of to-day is breaking up. Beyond this there is the need for some corporate body to direct and in some degree associate the multiple activities of medical minds of to-day. If some such joint association is not made effective there is a risk of the all-embracing State machine taking too great a part in controlling our activities. The need for some such organization was envisaged as long ago as 1905 by Sir Clifford Allbutt in his lecture, "The Historical Relations of Medicine and Surgery"; in that he formulated a plea for the foundation of an Academy of Medicine and proposed for it the Wriothesley motto of "Ung par tout et tout par ung." His ideas, I think, in some degree helped to advance the establishment of the Royal Society of Medicine; but this great foundation, successful as it is, does not supply the basis for that spiritual integration in an organized manner which is desirable if we are to present an undivided mind in face of State control and prevent the fragmentation of medicine into progressively smaller groups.

Duke-Elder in 1942 wrote, "British medicine in its present uncoordinated state, lacking central stimulation, guided by unrelated and often competing professional bodies and administered by a dozen Ministries, is in no position to assert itself in an integrated manner to confer the benefits it might upon the population, or to implement the opportunities of the immediate future in reconstruction, research, and international influence." This may exaggerate the incoherence of our present state, but, even if we reduce his dozen Ministries to one or two, it is not so far off the truth. In 1945 Duke-Elder again returned to the subject. He doubted the power of the Royal Colleges to fulfil their proper function if they remained separate and in some degree isolated, and he put the question: "If the practice of medicine becomes more and more an affair of the State, is the profession provided with a body powerful enough to preserve the soul of medicine in its personal and creative aspects without which it cannot live?"

Many members of this and the other Royal Colleges have, I know, felt the need of some such linking of the existing traditional organizations. Practical propositions were launched some years ago with great hopes, but unfortunately they foundered on the shoals of finance and divided counsels.

One cannot but feel that the spirit and heritage of Hunter, his great museum and our library, do constitute a focal point towards which a renewed effort might be directed to bring our forces together before we are utterly fragmented.

Conclusion

In accordance with the Orator's traditional privilege, I have strayed from my main subject, but I wished to show that the inspiration of Hunter was for the whole body of medicine, that the harvest he sowed matured slowly and has been but gradually garnered. If we look back on Hunter's work I think we may agree that he conformed to Francesco de Sanctis's definition of the man of science: "He is the highest and most virile type who needs no cult, for he carries the sentiment within him; he has no need for external stimuli for medals and titles, rewards or punishments . . . because he feels more powerful stimuli within him, and his conscience is stronger than any flag or banner."

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RELATION OF SHOCK, CARBOHYDRATE UTILIZATION, AND CORTISONE TO MITOTIC ACTIVITY IN THE EPIDERMIS OF THE ADULT MALE MOUSE

BY

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Green and Bullough (1950) showed that following hind-limb ischaemia or the injection of adenosine triphosphate (A.T.P.) there was an early and strong reduction, or complete suppression, of mitotic activity in the skin of the mouse. This powerful inhibition was shown to occur in the presence of a hyperglycaemia which in normal mice is associated with an increased mitotic rate (Bullough, 1949a). Thus we found further support for the hypothesis which one of us (with H. B. Stoner) had gradually evolved, that the state of shock is fundamentally a profound interference with carbohydrate utilization. It therefore became interesting to find what substances known to be operating in the shock mechanism, or, on the other hand, known to interfere in one or more stages of carbohydrate breakdown, were capable of inhibiting mitosis in the epidermis of the mouse. The typical feature of this action and those now to be described is that the affected cells cease to go into prophase though those already in it complete their divisions normally. The general methods have already been described (Bullough, 1948; Green and Bullough, 1950) and we can therefore proceed directly to the findings.

Hormones Released in the Response to Injury

It was suggested that, in view of the protective role of the suprarenal cortex in the response to injury, a hormonal factor from this source might be responsible for the mitotic inhibition found in shock (Green and Bullough, 1950). In an article suggesting a possible mode of action of A.C.T.H. in allergic conditions (Green,

1950) it was stated that A.C.T.H. had in fact a potent antimitotic effect. At the moment that statement must be modified in so far as all batches tested have not shown this property. We have reason to think that this lack of antimitotic effect reflects some general loss of biological activity. However that may be, there is no doubt that the more stable substance cortisone has a consistent and most powerful antimitotic action on the skin epithelium of the mouse (see Table).

Changes in the Epidermal Mitosis Rate of Mice (Kreyberg "White Label" Males) after Various Treatments

	No. of Mitotic Cells in 10 cm. of Ear Epidermis Cut 7 μ Thick							
Dose mg./10 g. Body Wt.	Cortisone	Controls	Dose mg./10 g. Body Wt.	Adrenaline	Controls	Dose mg./10 g. Body Wt.	Adenosine	Controls
0·1	12 (7·21)	53 (40·69)	0·004	6 (3·13)	—	3	14 (8·24)	68 (54·86)
0·5	0 (0·4)	88 (71·108)	0·01	20 (13·31)	—	3	20 (13·31)	82 (66·102)
1	13 (8·22)	56 (43·73)	0·02	0 (0·4)	—	3	12 (7·21)	110 (91·133)
2	0 (0·4)	52 (40·68)	0·04	2 (0·7)	62 (48·79)	3	·6 (3·13)	60 (47·77)
2	0 (0·4)	98 (80·119)	0·04	0 (0·4)	85 (67·106)	3	0 (0·4)	76 (61·95)
2	0 (0·4)	—	0·04	5 (2·12)	62 (48·79)			

All the drugs were administered intraperitoneally at 10 a.m. G.M.T. Control animals received an equivalent volume of 0·9% saline. All the counts were done on pieces of ear epidermis obtained at 2 p.m. G.M.T. Figures in brackets represent the 95% confidence intervals for the expected number of mitotic cells in 10 cm. (calculated on the basis of a Poisson distribution—that is, they give bounds to the purely chance variation of the number of mitotic cells counted).

Fairly strong inhibition was observed with parenteral doses of 0.1 mg. per 10 g. mouse. There is little doubt that some effect will be observed at a still lower dosage, for local painting of the cortisone suspension (25 mg./ml.) on one ear was sufficient to cause not only complete suppression of mitosis in the treated ear but also strong inhibition in the opposite ear.

As there is some evidence that adrenaline is one of the intermediary agents in the pituitary–adrenal response to injury (Long, 1947, 1949) and following A.T.P. injection (Stoner and Green, 1950) its effect was also studied, and it was found that it too depresses epidermal mitosis quite profoundly (see Table).

Other Substances Possibly Concerned in the Mechanism of Shock

Of these, A.T.P. and its derivatives most concern us here, for A.T.P. is known to have an antimitotic effect (Green and Bullough, 1950). The question remained open whether this was a specific property of the compound or one of the many reflections of its shock-inducing action with a concomitant stimulation of the pituitary–cortical mechanism (see Stoner and Green, 1950). To our surprise adenosine proved to be a powerful antimitotic agent *in vivo* in doses so far below the shock-inducing dose that little question of this being a non-specific action seemed possible (see Table). Moreover, Hughes in a personal communication stated that in tissue culture chick embryo fibroblasts showed a similar response both to adenosine and to adenyl compounds, which in biological concentrations prevented cells entering into the prophase of mitosis. Nor, on other grounds, did it seem likely that the effect of adenosine itself in the whole animal was due to the liberation of a cortical steroid with the antimitotic activity of cortisone; for adenosine, at the active antimitotic dosage, is unlikely to cause any significant suprarenal cortical discharge, at any rate in the rat (see Green and Stoner, 1950). Still more apposite is the fact that the skin of the adrenalectomized mouse responds to the antimitotic action both of adenosine and of A.T.P. (results will be published later).

We are left, therefore, with the provisional conclusion that, while A.T.P. injection in all probability exerts some of its antimitotic effect by causing discharge of cortical steroids, adenyl compounds in general have a direct antimitotic effect, or at least one not mediated through the suprarenal. Adenosine, though less active in this respect than its phosphorylated derivatives, causes a fall in general oxygen consumption and a transient fall in body temperature (Green and Stoner, 1950). Does adenosine, therefore, exert its antimitotic action by interfering in the respiratory cycle of carbohydrate utilization? Cortisone does not depress the body temperature but has a very powerful antimitotic action, and interference with the phosphorylation of sugar in the early stages of its glycolytic breakdown could explain this action.

What evidence is there that other agents capable of inhibiting any stage of carbohydrate breakdown interfere with mitosis? In tissue culture Hughes (1950) has reported on a variety of mitotic inhibitors, but only two —iodoacetate and fluoride, both inhibitors of glycolysis —completely suppressed mitosis in pre-prophase. Sodium fluoracetate, a powerful inhibitor in the carbohydrate respiratory cycle (see Peters, 1948), did not suppress mitosis in pre-prophase. *In vivo*, however, we have found in some preliminary experiments that all the three substances—sodium fluoracetate, sodium pyrophosphate, and iodoacetic acid—tested because they inhibit different phases of carbohydrate metabolism, showed mitotic inhibition in the pre-prophase stage.

Conclusions

In a preliminary report of this kind we would draw only general conclusions. The results tend to show that any significant interference with carbohydrate utilization at any stage, in the intact animal, prevents the epithelial cells of mouse skin from entering into the first stage of mitosis, possibly because all the energy build-up responsible for mitosis takes place in the pre-prophase stage (Bullough, 1949b). If this is so it provides supplementary evidence to the much more numerous and direct data (now being assembled) by the Sheffield Traumatic Shock Team suggesting that the state of shock is one of profound interference with carbohydrate utilization. It seems highly probable that the antimitotic effect of shock-inducing measures is due to this interference. The effect seems to be due in part to the liberation of a cortical steroid(s) which may interfere, possibly in the early stages, in the glycolytic breakdown of carbohydrate. Strong as this inhibition may be, judging from the antimitotic action of cortisone, it could not be the only way in which carbohydrate utilization is affected in the shock state, for, while A.C.T.H. and cortisone do not seriously affect the metabolic rate of the whole animal, a striking reduction in this rate is a cardinal feature of the shock state.

A working hypothesis on the basis of these mitosis counts is that in shock there are at least two inhibitory mechanisms affecting carbohydrate catabolism—one operating hormonally in the stage of glycolysis, and the other operating (possibly through the direct action of adenyl compounds) in the oxidative cycle. Stoner, Green, and Threlfall (1950) have already provided some chemical evidence of an interference with carbohydrate utilization in shock. Here we are mainly concerned to show how these studies may help to explain one aspect of the complicated action of cortisone and related steroids.

If the antimitotic effect is, as seems very likely, exerted on other tissues, such as the reticulo-endothelial, and in other species than the mouse, this powerful action must play a part (see Green, 1950) in the anti-allergic, anti-inflammatory, and anti-repair effects which in the mouse and rabbit, and possibly man, are so prominent. That such effects are incidental and not in any way linked up with the known therapeutic effects of cortisone and related substances is most unlikely. That they explain all the therapeutic effects is still less likely, for in that case adrenaline or A.T.P. should, in appropriate dosage, have the therapeutic virtues of cortisone, which they manifestly have not. The antimitotic effect of adrenaline is, however, interesting in view of its rather similar effects to A.C.T.H. and cortisone in reducing or abolishing some hypersensitive tissue reactions. This particular property is possibly due to the discharge, in excess, of a cortical steroid through adrenaline stimulation via the pituitary–adrenal route.

Summary

Cortisone, injected or applied locally, is a powerful inhibitor of mitosis in the pre-prophase stage in the epidermis of the adult male mouse.

Two other substances possibly concerned in the shock reaction—adrenaline and adenosine—when injected in adequate dosage have a similar action.

It is shown that these findings give indirect support to the hypothesis that in the shock state there is a profound interference with carbohydrate metabolism.

We are indebted to the Medical Research Council Committee on A.C.T.H., Cortisone, and Related Substances for supplying the cortisone, and to Mr. R. F. Wrighton, of the Department of Social Medicine, Sheffield University, for his valuable statistical help.

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Fresh water aboard ship has always been something of a problem, and its magnitude can be gathered from the fact that a modern liner uses about 220 tons a day in the Tropics, and must provide storage for 3,000 tons, representing a great loss in cargo capacity. The P. & O. are now for the first time to make all their fresh water by continuous distillation of sea water. In their new *Himalaya* special evaporators have been designed for heating by steam taken from the turbines after it has done its useful work there.

SHOCK AND NEOPLASIA

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It was shown (Green, 1949) that in the rat the growth of neoplasms from the time of transplantation was unaffected, or relatively unaffected, by repeated induction of the shock state, a procedure which powerfully inhibits mitosis in normal epidermis and probably many other tissues (Green and Bullough, 1950). This was unexpected, since the pronounced fall in oxygen consumption in the tissues of the shocked animal (Green and Stoner, 1950) and some retardation of general body growth might have been expected to retard neoplastic proliferation somewhat. Preliminary evidence was presented at the International Cancer Congress in Paris (Green, 1950) that, as might now be expected, the mitotic rate of the cells of the transplanted tumour was relatively unaffected by such a strong shock-inducing measure as hind-limb ischaemia or by the injection of A.C.T.H. Some further details are now presented together with an interesting extension of this inquiry. The general methods used have already been described (Bullough, 1948 ; Green and Bullough, 1950).

Tumour Mitosis and Natural Antimitotic Agents

Since then further investigations make it clear that such strong antimitotic agents as the shock state or injected cortisone (Green and Ghadially, 1951) do not affect mitosis in various transplanted tumours of mice and rats to anything like the same degree as is observed in the epithelium of normal skin.

In Table I some figures are abstracted from two typical experiments to show the effect and time-relationships of ischaemic shock and cortisone injection on the mitotic

TABLE I.—*Effect of Ischaemic Shock and Cortisone on Epidermal Mitotic Rates. Average Number of Mitoses per 10 cm. Length of Ear Epidermis in Sections Cut at 7 μ. The Figures Given are for 5 Strong's CBA Male Mice, and in the Case of Cortisone for 5 Kreyberg's "White Label" Male Mice*

Time of Day	Untreated Normal Mice	Ischaemic Shock. Removal of Limb Tourniquets at 11.30 a.m.	Cortisone, 0·2 mg. I.P. Injected at 12 noon
10.30 a.m. ..	31 ± 2·2	27 ± 2·9	—
12 noon	52 ± 4·1	14 ± 1·1	58·8 ± 14·2
1.30 p.m.	73 ± 1·2	0	9·2 ± 7·0
3 p.m.	44 ± 1·2	0	6·5 ± 3·6

rate in the skin of normal mice. In Table II the effect of similar treatments in tumour-bearing mice and rats on the mitotic rates of the tumours and of the epidermis in the same animal is illustrated. It has been found difficult in some instances to determine the effect of antimitotic agents on the skin of tumour-bearing mice, and the presence of a rapidly growing neoplasm may conceivably depress the rate of mitosis in normal epidermis. This point, however, is being investigated further, for, if true, it could be important. It will be readily seen, particularly if Tables I and II are compared, that the tumour mitotic rate in both the mouse and the rat is relatively unaffected as compared with the epidermal rate, either by ischaemic shock or by cortisone injection.

TABLE II.—*Effect of Ischaemic Shock and Cortisone on Epidermis and Tumour Mitotic Rates in the Same Tumour-bearing Animal. Average Number of Mitoses per 5 mm.² Tumour Section (5 μ) and 10 cm. of Ear Epidermis (7 μ) Taken at 3 p.m.*

Type	Tissue	Untreated Tumour Mice	Ischaemic Shock	Cortisone, 0·2 mg.
C3H male mice bearing breast carcinoma	Tumour	(10 Mice) 46·0± 3·2	(8 Mice) 36·6±5·0	(1 Mouse) 51
	Ear	15·5± 4·8	0	0
Wistar rats bearing RD3 sarcoma	Tumour	(8 Rats) 53·6± 1·8	(8 Rats) 25·6±2·6	—
	Ear	70·0±21·5	0·1	—

In some experiments ischaemic shock in the mouse did not reduce the tumour mitotic rate at all, and the most powerful reduction was only by about half as compared with complete suppression in the epidermis.

It must be recognized, of course, that we are not comparing the malignant cell with its normal prototype —that is, skin carcinoma with skin epithelium. There is, however, collateral evidence from human studies with A.C.T.H. and cortisone which seem to us to indicate that neoplasms of the lymphoid tissues are not so sensitive as normal lymphoid tissue to the "involuting" effect of these substances. Though striking shrinkage of enlarged lymph nodes was observed in chronic lymphatic leukaemia, lymphosarcoma, etc. (Pearson and Eliel, 1950), this was usually transitory and may have been due partly to "involution" of normal hyperplastic lymphoid tissue. It is perhaps significant that a variety of neoplasms, both carcinomata and sarcomata, were completely unaffected by this treatment. There is probably a relationship between this lack of response of many human malignant neoplasms to cortisone and A.C.T.H. and the relatively weak or negligible antimitotic effect observed in our animal neoplasms. If it could be generally established, a negative might prove of greater interest than a positive effect by revealing an essential difference, amenable to experimental approach, between the normal and the malignant cell. One approach we are trying is to treat chemically induced carcinomata of the skin in mice with cortisone, as cortisone has a definite local antimitotic effect on normal mouse skin (Green and Ghadially, 1951).

Another and perhaps more practical approach was to find the response of the skin pretreated with a chemical carcinogen to these powerful antimitotic agents. Does such a local treatment make the epithelium refractory to such agents in whole or in part? We have now good evidence that it does. After a short period (not more than four paintings over eight days) of treatment with the powerful carcinogen 9 : 10-dimethyl-1 : 2-benzanthracene (D.M.B.), the mitotic rate of the ear epidermis usually rises quite substantially above the normal rate and above that of the opposite ear treated with the solvent only. The high rate is maintained for some days after cessation of the painting, but appears to decline with the gradual disappearance of the increased vascularity produced locally by the treatment. This increase in the mitotic rate is rarely, though it is occasionally, as great as after croton-oil painting (see Table III).*

From the present standpoint this stimulant effect of the carcinogen is by no means so important as the response of the treated cells to shock-inducing measures

*The experiments with croton oil were done in collaboration with Dr. W. S. Bullough.

TABLE III.—*Response to Antimitotic Agents of Ears Treated with 9 : 10-Dimethyl-1 : 2 Benzanthracene (0.5% in Acetone) and Croton Oil (1% in Acetone). Five Kreyberg's "White Label" Male Mice were Used in Each Case*

No. of Paintings	Average No. of Mitoses per 10 cm. of Ear Epidermis (7 μ)				
	Day of Count	Antimitotic Agent	Time of Day	L. Ear (Control)	R. Ear (Treated)
D.M.B.; 4 applications over 9 days	9th	Ischaemic shock tourniquets released at 12.30 p.m.	10.30 a.m.	13·0± 4·0	31·2± 6·4
			4.30 p.m.	0	42·3± 6·8
D.M.B.; 4 applications over 8 days	8th	" "	10.30 a.m.	3·8± 1·2	29·6±11·8
			4.30 p.m.	0	36·6±13·1
D.M.B.; 4 applications over 8 days	8th	Cortisone (0·2 mg.) I.P. at 12 noon	12 noon	58·8±14·2	54·6±12·0
			3 p.m.	6·5± 3·0	44·8±10·0
Croton oil; 5 applications over 10 days	10th	Ischaemic shock tourniquets released at 11.30 a.m.	10.30 a.m.	26	293
			3 p.m.	0	3

and physiologically equivalent procedures. In Table III examples are given of typical experiments. The carcinogen-treated ear, in contrast to the untreated opposite ear, showed only a slight response to the decisive antimitotic stimulus following the release of limb tourniquets (Green and Bullough, 1950) or following the injection of cortisone (Green and Ghadially, 1951). In striking contrast is the effect of shock on the hyperplastic epithelium induced by croton oil (Table III). Here the excessively high mitotic rate was almost completely suppressed, though not quite so quickly as was normal mitosis in the untreated opposite ear.

Discussion

Two most interesting conclusions can be drawn from this work at its present stage.

Even a relatively short exposure (in terms of tumour development) to a chemical carcinogen makes the skin epithelial cells refractory in some degree to the antimitotic action of certain natural agents. The skin is now relatively insensitive to the profound antimitotic effect of induced shock. Of the known factors concerned in this effect only cortisone and A.C.T.H. have been tested, and the carcinogen-treated skin was refractory to both. We are, however, at the moment somewhat uncertain of the biological potency of the sample of A.C.T.H. used. Adenosine and its compounds have not yet been tested, but, as their effects are in the present respect exactly like those of shock (Green and Bullough, 1950; Green and Ghadially, 1951), the same lack of response in the carcinogen-treated skin may be anticipated. It is also highly significant that the abnormally high rate of mitosis induced by croton oil is nearly as responsive to shock inhibition as is normal skin. The contrast here between the behaviour of the cell involved in the inflammatory reaction and the cell involved in the "precancerous" reaction is remarkable.

If the skin paintings are stopped, at any rate at an early stage, the refractory state to these agents inhibiting cell division gradually disappears. We do not know as yet if, and at what stage of treatment, the refractory state becomes permanent. That it does become permanent is highly probable, for in a considerable number of tests on three neoplasms (a breast carcinoma and two types of chemically induced sarcomata) the maximum decrease in the mitotic rate following a strong shock

stimulus was only a half. In many instances the malignant cell appeared to be completely refractory to such stimuli. Of course the importance of this finding depends on how far it reflects an essential difference betweeen the malignant cell and its normal prototype. The effects of local carcinogen treatment do, however, strongly suggest that the resistance of the fully developed cancer cell is acquired very early in neoplasia and gradually becomes a permanent property of the cell.

Although such a resistance to normal growth-regulating agents has often been postulated as a property of the cancer cell, and in fact is vaguely included in one definition—that is, "autonomous new growth"—the property has never been precisely demonstrated experimentally. It may be that this work not only reveals the existence of such a property but offers an approach to an elucidation of its nature. If, as we think (Green and Bullough, 1950; Green and Ghadially, 1951), these antimitotic agents act on the normal cell by interfering at one or more stages in carbohydrate utilization, the work of the Sheffield Traumatic Shock Team on carbohydrate metabolism in shock may prove to have some bearing not only on the mechanism of this general bodily reaction but also, somewhat surprisingly, on the intimate changes in cell metabolism, which in themselves reflect, or constitute, the essential nature of neoplastic transformation.

Summary

A short period of painting of the ear with the carcinogen 9:10-dimethyl-1:2-benzanthracene renders the epidermis relatively refractory to the antimitotic action of shock or of cortisone.

Various transplanted malignant neoplasms are also relatively insensitive to the same stimuli.

Whether these findings have a bearing on the essential nature of the neoplastic change is briefly discussed.

We are indebted to the Medical Research Council Committee on A.C.T.H., Cortisone, and Related Substances for supplying the cortisone; to Mr. R. F. Wrighton, of the Department of Social Medicine, Sheffield University, for his valuable statistical help; and to Dr. W. S. Bullough for his expert collaboration in one experiment.

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How the honey-bee discovers the first, newly opened flowers of a crop was discussed in a paper read to the Royal Society on March 8 by Dr. C. G. Butler, of Rothamsted Experimental Station, Harpenden. It has been known for a long time that bees possess good colour vision, though they can see into the ultra-violet where the human eye is blind and are insensitive to red—whence, it is suggested, arises the scarcity of pure red flowers. More recently Professor Karl von Frisch has described the amazing dance a scout bee performs on returning to the hive to let its worker colleagues know where it has found a new group of open flowers with pollen and nectar ready. But how does the scout discover the new flowers in the first instance—by sight or smell? Dr. Butler reported that colour is the chief attractive factor, though a really strong perfume acts in the same way. The scent of an individual flower is, however, often weak, and it serves only to induce the honey-bee to enter the corolla once the colour has done its work. If the scent is masked, the bee hesitates to enter on the first or subsequent visits.

CHEMOTHERAPY IN CHOLERA

BY

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Really effective chemotherapy in cholera has hitherto proved to be a baffling problem. However, good results have been claimed for a few of the newer compounds. Among these, sulphaguanidine has been extensively used for the past few years, but opinions regarding its efficacy in this disease have not been uniform (Chopra *et al.*, 1941; Carruthers, 1942; Lahiri, 1945, 1948). In another series of observations (Lahiri, 1949; Lahiri and Dutta, 1949) thiodiamine was tried. This is derived from the decomposition product of the bark of *Crataeva roxburghii* and also of *Moringa pterygosperma*. *In vitro* it prevented the growth of *Vibrio cholerae* (both Ogawa and Inaba types) even in a concentration of 0.5 mg. in 10 ml. of media. On clinical trial in 30 bacteriologically positive cases the stool became free of vibrio in three to five days in all the 23 cases systematically observed, but the death rate was not materially lowered.

Bhatnagar *et al.* (1948) had remarkably good results with another compound—a condensation product of sulphathiazole and formaldehyde. Out of 85 patients treated with this drug in a part of the Madras Presidency during an epidemic in 1947 only three died (3.53%): the case mortality rate had been about 60% in epidemics during the previous seven years. Saline transfusion was not given to any of these patients, and there was no nursing and general medical care or adjuvant treatment, though 57 patients (67.06%) were in a critical condition with anuria, marked dehydration, "semi-comatose condition, algidity, imperceptible pulse, and body cramps." Stools became free from vibrio in all the cases within six days. The prophylactic value of this drug has also been emphasized. Bose (1949), in experiments *in vitro* with different condensation products of formaldehyde and sulphonamides, found that formosulphacetamide and formosulphabenzamide exerted better bactericidal effect on *V. cholerae* than formosulphathiazole and other similar compounds.

A clinical trial of some of the above compounds—for example, sulphaguanidine, formosulphathiazole, and formosulphacetamide—was undertaken in cholera cases admitted into the cholera ward of the Chittaranjan Hospital, Calcutta, during the last epidemic (1950). The findings are discussed below.

Clinical Investigation

The period of observation of the cases discussed here was from May to July, 1950. The total number of patients admitted during this period was 377, and there were 122 deaths (32.35%). Many of these patients were refugees in a bad state of nutrition and with lowered vitality. Consequently the death rate was high. A total of 268 patients were under clinical observation for the present study. All these patients presented typical symptoms of cholera, with profuse rice-water stools, vomiting, and dehydration with anuria, prostration, and high specific gravity of blood. At the time of admission 133 patients (49.62%) were in a very bad state of collapse, with imperceptible radial pulse and the specific gravity of blood varying between 1068 and 1072.

Powdered sulphaguanidine, formosulphathiazole, and formosulphacetamide were given orally to successive patients in cyclic order according to their admission into the ward, the fourth one admitted receiving no chemotherapeutic drug, and thus serving as a control. But this order could not always be strictly maintained owing to irregular supply of drugs and other difficulties. Of the 268 patients, 72 received sulphaguanidine, 64 formosulphathiazole, 61 formosulphacetamide, and 71 were controls. All received adjuvant treatment.

Dosage.—The dosage was the same for all three compounds—4 g. initially, followed by 2 g. every four hours throughout the day and night for an adult, till the symptoms subsided or the stool became vibrio-free. Children received proportionately lower doses according to age. During the first few days of the investigation the dosage for both formosulphathiazole and formosulphacetamide was 2 g. initially, followed by 1 g. every four hours, but this was subsequently increased for want of any beneficial response with this dosage schedule. Adjuvant treatments were given to all the patients when necessary.

Adjuvant Treatments.—All patients received saline transfusion (hypertonic, isotonic, and alkaline) till the specific gravity of the blood came down to normal level. Atropine sulphate, 1/100 gr. (0.65 mg.) hypodermically, was given to all adult patients on admission, and was repeated after 8 to 12 hours as necessary, All the patients received glucose intravenously either in the form of 25% solution, 50 ml. every eight hours, or with normal saline in 5% solution as transfusion, children receiving a proportionately less quantity. As an analeptic nikethamide was extensively used, intravenously in grave cases, and intramuscularly otherwise, and also extract of suprarenal cortex when available (Lahiri, 1945). Compounds of theophyllin were used intravenously in many cases to stimulate urination. To combat the persistent collapse a number of patients belonging to all the four groups received plasma or Knox special intravenous 6% gelatin solution intravenously. The result of the latter observation is being published elsewhere.

Examination of Stools

Stool was collected by a sterile rubber catheter direct from the rectum of the patient into a test-tube containing alkali-peptone media solution, and sent to the laboratory. The first sample was taken before giving any chemotherapeutic drugs. Subsequent samples were taken on successive days, in the same way, to study the bactericidal effect of the drug used or as controls. Altogether 745 samples of stools were cultured in this series.

Results

V. cholerae was found in the stools of 197 cases (73.5%) (Table I). These were all typical *V. cholerae* belonging to Heiberg's group 1 category. Serological investigation with monospecific sera showed initially:

TABLE I.—*Results of Treatment*

	No. of Cases	Deaths	
		No.	%
Investigated	268	78	29·1
Vibrio-positive (V+)	197	54	27·41
Ogawa cases	142	39	27·46
Inaba cases	51	11	21·56
Admitted with imperceptible radial pulse (P−)	133	57	42·85
Vibrio-positive, admitted with imperceptible radial pulse (V+, P−)	109	45	41·28
Vibrio-negative (V−)	71	24	33·8
Vibrio-negative, admitted with imperceptible radial pulse (V−, P−)	24	12	50·0

(*a*) type Ogawa in 142 samples (72.08%), (*b*) type Inaba in 51 samples (25.88%), and (*c*) four were not investigated. In 29 cases (14.72%) culture of the first sample of stool failed to reveal any vibrio, though subsequent examinations demonstrated the vibrio.

The effects of sulphaguanidine, formosulphathiazole, and formosulphacetamide therapy, and also of control with no chemotherapeutic drugs, were studied in this series in 72, 64, 61, and 71 patients respectively, the respective case mortality rates being 30.55%, 34.37%, 34.43%, and 18.31% (Table II). In severe cases admitted with imperceptible radial pulse, death rates

TABLE II.—*Analysis of Results of Treatment*

Cases	Sulphaguanidine			Formosulphathiazole			Formosulphacetamide			Nil		
	No.	Deaths		No.	Deaths		No.	Deaths		No.	Deaths	
		No.	%		No.	%		No.	%		No.	%
V+	51	15	29·41	50	17	34·0	44	12	27·27	52	10	19·23
Ogawa	34	10	29·41	42	15	35·71	29	7	24·14	37	7	18·92
Inaba	15	3	20·0	8	2	25·0	13	3	23·07	15	3	20·0
V−	21	7	33·33	14	5	35·71	17	9	52·94	19	3	15·78
P−	31	14	45·16	41	20	48·75	30	13	43·33	31	10	32·26
V+P−	28	12	42·86	34	16	42·66	23	9	39·13	24	8	33·33
Total	72	22	30·35	64	22	34·37	61	21	34·43	71	13	18·31

V+ = *V. cholerae* present in stool. V− = *V. cholerae* absent in stool. P− = Admitted with imperceptible radial pulse. V+P− = Vibrio-positive cases admitted with imperceptible pulse.

TABLE III.—*Analysis of Results According to Age Group*

Age in Years	Sulphaguanidine				Formosulphathiazole				Formosulphacetamide				Nil			
	No.	No. P−	Deaths		No.	No. P−	Deaths		No.	No. P−	Deaths		No.	No. P−	Deaths	
			No.	%			No.	%			No.	%			No.	%
0–4	9	3	3	33·33	1	1	1	100·0	0	—	—	—	3	0	0	0·0
5–9	5	3	2	40·0	2	0	0	0·0	3	2	3	100·0	0	—	—	—
10–19	12	6	2	16·66	13	9	5	37·46	10	3	2	20·0	18	5	1	5·5
20–39	36	17	12	33·33	38	24	9	23·68	41	19	12	29·27	40	20	9	21·9
40–49	5	1	3	60·0	5	4	1	20·0	3	3	3	100·0	4	4	0	0·0
50–59	3	0	0	0·0	5	3	3	60·0	2	2	1	50·0	4	1	1	25·0
60+	2	1	0	0·0	0	—	—	—	2	1	0	0·0	2	1	2	100·0

were 45.16%, 48.75%, 43.33%, and 32.26% respectively, respective numbers of cases being 31, 41, 30, and 31. In the studies of age groups (Table III) the lowest mortality rates were also obtained in the control group. This was true both for vibrio-positive and vibrio-negative patients. Among those receiving formaldehyde condensation products the mortality was a little higher than among those receiving sulphaguanidine.

Table IV reveals that the largest percentages of deaths in all the groups were due to peripheral circulatory failure. In these patients the systolic blood pressure failed to rise above 70–80 mm. Hg, or it dropped down again after a slight temporary rise, though the specific gravity of the blood was brought down to normal level by rapid intravenous saline transfusion, followed by the continuous slow-drip method as long as required. The next most frequent cause of death was uraemia, the formol compound groups recording higher percentages than the other two groups.

TABLE IV.—*Causes of Death (Clinical)*

Treatment	No. of Deaths	Causes of Death					
		Peripheral Circulatory Failure		Uraemia		Other Causes	
		No.	%	No.	%	No.	%
Sg ..	22	12	54·54	5	22·72	5	22·72
FST ..	22	11	50·0	11	50·0	0	0·0
FSA ..	21	10	47·61	7	33·33	4	19·04
Nil ..	13	9	69·23	3	23·07	1	7·69
Total	78	42	53·84	26	33·33	10	12·82

Effects on V. cholerae in the Stool

This was studied in 130 cases. The stools from 33 patients taking sulphaguanidine, 34 taking formosulphathiazole, 27 taking formosulphacetamide, and 36 having no chemotherapeutic drugs were examined systematically from day to day to study the effects of these drugs on *V. cholerae* (Table V). On the eighth day from the onset vibrio disappeared from the stool in 32 patients (96.93%) in the first group, 32 (94.11%) in the second group, 26 (96.29%) in the third group, and 30 (83.3%) in the control group. All the stools became vibrio-negative by the ninth day in the first group, by the tenth day in the third group, and by the twelfth day in the control group. In the formosulphathiazole group, one patient, who still had *V. cholerae* in the stool on the tenth day, after taking 72 g. of the drug, became symptom-free and left hospital.

The average amount of these drugs received before the stools became vibrio-negative was not at all uniform, larger total quantities being taken as a matter of course as the number of days increased. In some cases the stools became vibrio-negative one or two days after the drugs were discontinued, though they were positive all the time the drugs were being taken. In 18 patients in the whole series, distributed in all the four groups, it was noticed that the vibrio, while present in the stool on one day, was absent again for one or more days, and then reappeared, though the respective treatments were being continued. The longest interval observed was four days in a patient in the control group.

Another interesting fact observed was the alteration of the serological types of the *V. cholerae in vivo*. This occurred in 24 patients, and was not influenced by chemotherapy. Though the question of chance contamination cannot be entirely ruled out in all the cases in this series, in some cases a particular serological type was the only one of its kind isolated that day. A few examples of mutation are given in Table VI.

TABLE V.—*Analysis of Results of Treatment on V. Cholerae in Human Stool*

Day When Vibrio-Free	Sulphaguanidine					Formosulphathiazole					Formosulphacetamide					Nil				
	Total Cases Freed				Av. Quantity Drug Required (g.)	Total Cases Freed				Av. Quantity Drug Required (g.)	Total Cases Freed				Av. Quantity Drug Required (g.)	Total Cases Freed				Av. Quantity Drug Required (g.)
	Ogawa	Inaba	V+	%		Ogawa	Inaba	V+	%		Ogawa	Inaba	V+	%		Ogawa	Inaba	V+	%	
2nd ..	0	1	1	3·03	10·0	0	1	1	2·94	9·0	1	0	1	3·7	6·0	2	0	2	5·5	0
3rd ..	2	2	4	12·12	18·25	5	1	6	17·64	14·6	5	1	6	22·2	18·5	3	1	4	11·1	0
4th ..	6	4	10	30·3	22·16	7	1	8	23·52	25·2	3	3	6	22·2	22·0	7	4	11	30·5	0
5th ..	1	0	1	3·03	25·0	4	3	7	20·58	35·6	6	3	9	33·3	20·0	6	1	7	19·4	0
6th ..	10	3	13	39·39	32·07	3	0	3	8·82	36·4	0	1	1	3·7	6·0	2	1	3	8·3	0
7th ..	1	1	2	6·06	28·5	3	0	3	8·82	32·6	3	0	3	11·1	33·3	1	0	1	2·7	0
8th ..	1	0	1	3·03	21·0	4	0	4	12·35	50·5	0	0	—	—	—	1	1	2	5·5	0
9th ..	1	0	1	3·03	50·0	0	0	—	—	—	0	0	—	—	—	2	0	2	5·5	0
10th ..	—	—	—	—	—	0	1	1	2·94	27·0	0	1	1	3·7	13·0	1	1	2	5·5	0
11th ..	—	—	—	—	—	1*	0	1	2·95	72·0	—	—	—	—	—	—	—	—	—	—
12th ..	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	1	2	5·5	0
Total V+ studied			33					34					27					36		

* This patient, though still showing *V. cholerae* (Ogawa) in the stool on the tenth day after 72 g. of formosulphathiazole, became symptom-free and left hospital.

TABLE VI.—*Example of Alteration of Serological Types of V. Cholerae During Treatment*

Case No.	Treatment	Amount Used before V–	Examinations								Remarks
			1st	2nd	3rd	4th	5th	6th	7th	8th	
A	Sg	50 g.	Ogawa	Nil	Ogawa	*Ogawa	Inaba	Nil	Nil	Nil	*Ogawa + after 50 g.; drug stopped; then Inaba; then nil
B	FST	40 g.	Inaba	Ogawa	Inaba	Inaba	Hikojima	Nil	Nil	Nil	Out of 415 strains serologically tested Hikojima was present in only one sample
C	FSA	26 g.	Inaba	Inaba	Ogawa	Nil	Nil	Nil	Nil	Nil	
D ..	Nil		Inaba	Inaba	Inaba	Inaba	Inaba + Ogawa	Inaba + Ogawa	Inaba	Nil	

Blood Concentration of the Drugs

Systemic absorption of the different chemotherapeutic drugs used in this series was studied by estimating their concentration in the blood, in terms of free and total sulphonamide (Table VII). This was estimated in

TABLE VII.—*Serum Concentration of Sulphaguanidine (Sg), Formosulphathiazole (FST), and Formosulphacetamide (FSA) in Terms of Sulphonamide in mg. per 100 ml.*

Case No.	Treatment	Total Quantity and in Days	Sulphonamide Concentration mg./100 ml.		Urinary History
			Free	Total	
1	Sg	26 g. 3 days	2·1	2·9	1st urine after 24 hours, then free
	Sg	50 g. 6 days	1·4	1·5	Free urine
2..	Sg	58 g. 6 days	2·1	2·2	1st urine after 12 hours, then free
3..	Sg	36 g. 4 days	12·5	13·9	1st urine after 48 hours; then scanty for two days, then free
4..	FST	13 g. 2 days	0·64	1·4	No urination; died
5..	FST	64 g. 6 days	0·75	1·5	Urine showed sulphanilamide (free 12·5, total 13·5 mg. per 100 ml.)
6..	FST	72 g. 8 days	0·4	1·2	1st urine after 21 hours, then free
7..	FST	56 g. 9 days	2·5	4·2	1st urine after 53 hours, then free
8..	FST	52 g. 5 days	Not detectable	Not detectable	Free urine, after 12 hours
9	FST	32 g. 3 days	2·1	2·2	1st urine after 30 hours, then free
	FST	54 g. 6 days	0·46	0·6	Free urine
10..	FST	23 g. 4 days	0·87	1·1	1st urine after 24 hours, then free; cured
11..	FST	14 g. 3 days	0·60	1·1	1st urine after 48 hours, followed by anuria; died
12..	FST	44 g. 7 days	0·35	0·54	1st urine after 12 hours, then free; cured
13..	FST	19 g. 6 days	0·37	0·63	1st urine after 24 hours, then free; cured
14..	FSA	24 g. 3 days	6·0	14·4	No urination; died
15	FSA	24 g. 2 days	2·4	2·6	1st urine after 18 hours, then free
	FSA	53 hrs., after 36 g.	0·71	0·87	Free urine
16..	FSA	30 g. 4 days	2·1	2·96	1st urine in 24 hours, then free
17..	FSA	8 g. 1 day	0·8	1·1	No marked anuria
18..	FSA	17 g. 2 days	2·0	5·5	1st urine after 28 hours, then free; cured
19..	FSA	18 g. 6 days	1·7	4·5	No urine; died
20..	FSA	36 g. 4 days	3·7	5·7	1st urine after 24 hours, then free; cured

three patients having sulphaguanidine, ten patients having formosulphathiazole, and seven patients having formosulphacetamide. The average blood sulphonamide concentration for formosulphacetamide was free 2.42 mg. and total 4.7 mg., and for formosulphathiazole free 0.82 mg. and total 1.31 mg. per 100 ml. of blood ; the respective total quantities of drugs received were 24.12 g. and 40.27 g. in four and five days respectively.

One patient having sulphaguanidine, with prolonged anuria followed by scanty urination, showed a high blood concentration (free 12.5 mg. and total 13.9 mg. per 100 ml.). Except for this case formosulphathiazole showed the lowest and formosulphacetamide the highest blood concentrations. In several instances the importance of free urination in keeping the blood concentration low was apparent. A sample of urine from a patient having formosulphathiazole showed fairly high excretion figures (12.5 and 13.5 mg. per 100 ml.). Formosulphacetamide was detectable in the blood of one patient examined 53 hours after discontinuation of the drug.

Discussion

In the present series sulphaguanidine, formosulphathiazole, or formosulphacetamide did not reduce the mortality rate of cholera patients, the rate being lowest in the group that did not receive chemotherapy. This latter fact was noticeable not only in vibrio-negative but also in vibrio-positive cases, and even in patients admitted in a serious condition with no perceptible radial pulse. On an analysis of the causes of death it was noticed that the highest mortality was due to peripheral circulatory failure in all the groups. The next most frequent cause was uraemia, which was more apparent in patients getting the formaldehyde compounds.

The failure of chemotherapy in cholera is not altogether unexpected from the nature of the disease itself, with its sudden onset and profuse vomiting and purging, which rapidly produce a condition of marked dehydration and serious systemic biochemical changes. There also occurs a great fall in the systolic blood pressure, resembling shock. It is not only the loss of systemic fluid but also the absence of sufficient filtration pressure in the glomeruli of the kidneys that produces the anuria. In many cases a quick supply of fluid and salt rapidly improved both dehydration and the low blood pressure, but in others, especially in late cases, circulatory collapse becomes irreversible. Chemotherapy cannot be expected to influence the above condition except possibly by way of prevention of the development of the disease initially. Once the disease is fully developed the most important factor in its treatment is undoubtedly an adequate supply of fluid and salt, and efforts should be made to prevent collapse becoming irreversible.

Analysis of the effects of the different chemotherapeutic compounds on *V. cholerae* in human stool in this series does not show any appreciable vibriocidal result *in vivo* when compared with the control group having no chemotherapy. In day-to-day observations regarding the numbers of persons becoming vibrio-free, from the second day onward the control group showed practically the same results as the groups having chemotherapeutic treatment, slight differences being negligible. If the vibrio disappears from the stool at practically the same rate without chemotherapy as with it, then the sulphonamides used in this series cannot be of much practical value.

In some patients it was observed that the vibrio continued to be present in the stool so long as the drug was being administered, but disappeared one or two days afterwards. This fact also demonstrates that time is more important for the disappearance of the vibrio from the stool than the quantity of chemotherapeutic drugs given. In the absence of any appreciable vibriocidal effects of these drugs *in vivo*, their prophylactic value cannot be of any significance. Another point noted was that, once the symptoms of cholera developed, the death rate was also high among patients who showed no *V. cholerae* in their stools.

Estimation of blood sulphonamide concentration showed that all the drugs used in this series were absorbable even at the height of the disease, though least absorption occurred with formosulphathiazole. A sulphonamide may be an additional burden on the already dysfunctioning excretory system, especially if associated with irritant compounds like formaldehyde, as may be seen in increased mortality figures for uraemia in persons receiving the latter drug. On serological typing it was found that most positive cases were

infected with the Ogawa type of organism. The death rate was also higher in that type. Mutations of the serological types are little-understood phenomena. These were not abolished by chemotherapy.

Conclusion

Sulphaguanidine, formosulphathiazole, and formosulphacetamide given orally did not reduce the mortality rate in cholera patients, and results in these cases compared unfavourably with those in cases where no chemotherapy was given; other treatment remained the same. No special vibriocidal effect of these compounds was apparent *in vivo*, the *V. cholerae* disappearing from the stools practically at the same rate, both in those who had chemotherapy and in those who had none. In assessing the value of the vibriocidal effect of any drug in this disease *in vivo*, it is important to note that the *V. cholerae* disappears from the human stool automatically at a fairly quick rate. This disease characteristically comes on and passes off like a storm, and once it is fully developed the most important part of treatment is undoubtedly to replace quickly the fluid and salt lost and to prevent the development of the irreversible condition of circulatory collapse. This peripheral circulatory failure is an important cause of persistent anuria occurring as a result of failure of adequate glomerular filtration pressure, which ultimately leads to complete renal failure. Chemotherapeutic drugs, to be of any real value in cholera, must have a quicker action than any of the sulphonamides tested in this series, and also should not be toxic.

My thanks are due to Mr. P. N. Sen Gupta, of Bengal Immunity Research Institute, for bacteriological work; to Dr. A. N. Bose, of the same institute, for estimating the blood sulphonamides; and to the Director of the Institute, Dr. U. P. Basu, for supplying free of cost the sulphacetamide used and for allowing the investigations to be carried out there. Thanks are also due to Messrs. Ciba Pharma Ltd. for supply free of cost the formosulphathiazole, in the form of "formocibazole." I am grateful to my house-physicians and nursing staff, but for whose untiring co-operation during an epidemic this work would not have been possible.

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The Tavistock Clinic, as an out-patient hospital dealing with psychological problems of individuals and families, has been absorbed in the National Health Service, but a branch of it known as the Tavistock Institute of Human Relations has been incorporated as a separate social research organization concerned with the psychology of relations between human beings in domestic, industrial, and civic groups. It is governed by a council of eight, four of whom are medical, and the council is responsible to an association of 50 members elected on a basis of professional activity or interest in applied social research. In a small brochure recently issued from 2, Beaumont Street, W.1, an account is given of four years' work. About 70 projects of different kinds have been undertaken, some of them for government departments or local authorities, others for industrial concerns or voluntary organizations interested in community and family affairs. To name a few: a study of some aspects of resettlement in the British zone of Germany; the design of a medical statistics service in a local health authority; the job analysis of nursing auxiliary roles in a hospital group; the development of a new type of family case-work agency; the assessment of safety education films for children.

THE INCIDENCE AND PREVENTION OF TETANUS AMONG CIVILIANS

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Tetanus is not a notifiable disease in England and Wales, and the only useful indication of its general incidence is that obtainable from the mortality statistics of the General Register Office.

Recent Trend of Mortality

Table I gives the numbers of registered deaths and the death rates from 1931 to 1948, and the latter are illustrated in Fig. 1. (See footnote to Table I regarding exclusion of non-civilians.) The male death rate has recently shown a definite tendency to decline, and the rates during 1946–8 were about half of those recorded between 1931 and 1940. Female rates, on the other hand, remained fairly steady, declining only very slightly during the period.

TABLE I.—*Deaths From Tetanus and Death Rates Per Million Living by Sex. England and Wales, 1931–48*

Year	Males		Females	
	No. of Deaths	Rate per Million Living	No. of Deaths	Rate per Million Living
1931	92	4·8	25	1·2
1932	93	4·8	21	1·0
1933	74	3·8	28	1·3
1934	85	4·4	26	1·2
1935	98	5·0	28	1·3
1936	86	4·4	29	1·4
1937	85	4·3	22	1·0
1938	72	3·6	17	0·8
1939	62	3·1	23	1·1
1940	91	5·0	18	0·8
1941	79	4·6	20	0·9
1942	66	3·9	29	1·4
1943	61	3·7	24	1·1
1944	55	3·4	33	1·5
1945	55	3·4	24	1·1
1946	41	2·2	22	1·0
1947	49	2·5	22	1·0
1948	48	2·4	21	0·9

Note.—This and subsequent tables exclude non-civilian males on and after September 3, 1939, and non-civilian females on and after June 1, 1941.

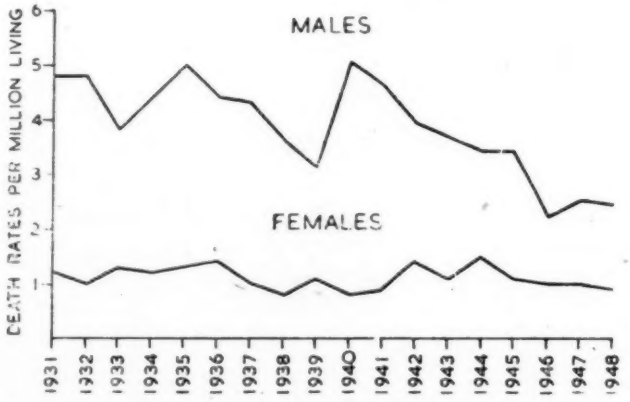

FIG. 1.—Annual death rates from tetanus per million living at all ages. England and Wales, 1931–48.

Sex and Age Incidence in 1928–37 and 1938–47

Table II compares deaths and mean annual death rates by sex and age during the two decennia 1928–37 and 1938–47, these death rates being illustrated in Fig. 2. Only in boys aged between 1 and 10 were the death rates higher in the second of the two decennia. In each sex the mortality was highest during infancy and childhood, lowest during the middle years of life, rising again after 50, especially among males. The death rates among males at every age in both decennia were much higher than the corresponding female rates; in 1938–47 they ranged from 1.7 times the female rate under 1 year of age to 11 times at 75 years and over.

TABLE II.—*Deaths From Tetanus and Mean Annual Death Rates Per Million Living by Sex and Age. England and Wales, in Each of the Two Decennia 1928–37 and 1938–47*

Age Group	Males				Females			
	1928–37		1938–47		1928–37		1938–47	
	No.	Rate	No.	Rate	No.	Rate	No.	Rate
0– ..	25	8·3	23	6·9	12	4·1	13	4·1
1– ..	39	3·3	44	3·7	23	2·0	21	1·8
5– ..	86	5·3	93	6·5	30	1·9	25	1·8
10– ..	143	8·6	76	5·2	31	1·9	14	1·0
15– ..	77	4·7	41	3·0	13	0·8	10	0·6
20– ..	75	4·4	15	1·8	15	0·9	14	0·9
25– ..	66	4·0	17	1·6	17	1·0	13	0·8
30– ..	56	3·7	21	1·6	22	1·3	14	0·8
35– ..	43	3·2	32	2·2	17	1·1	20	1·2
40– ..	51	4·1	40	2·9	20	1·4	11	0·7
45– ..	39	3·3	40	3·2	15	1·1	6	0·4
50– ..	57	5·1	28	2·4	13	1·0	15	1·1
55– ..	55	5·5	32	3·0	18	1·6	14	1·1
60– ..	62	7·7	51	5·5	16	1·7	16	1·4
65– ..	32	5·3	37	5·0	11	1·5	17	1·9
70– ..	28	7·1	26	5·0	7	1·4	6	0·9
75+ ..	15	4·5	21	4·5	5	0·9	3	0·4
Total ..	949	4·9	637	3·6	285	1·4	232	1·1

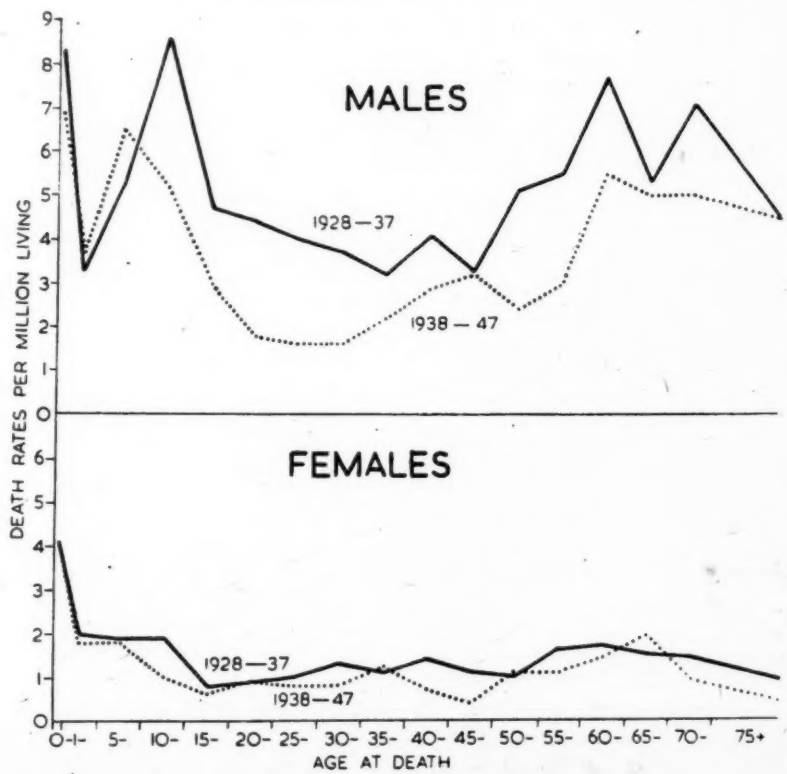

FIG. 2.—Mean annual death rates from tetanus per million living. Males and females by age. England and Wales, 1928–37 and 1938–47.

Mortality Among Infants.—Table III shows the deaths of 36 (23 males, 13 females) infants between 1938 and 1947 by sex and age in months—29 were under 1 month.

TABLE III.—*Deaths From Tetanus Under 1 Year, by Sex and Age in Months, England and Wales, 1938–47*

Year	Sex	Months												Total
		–1	1	2	3	4	5	6	7	8	9	10	11	
1938	M	—	—	—	—	—	—	—	—	—	—	—	—	—
	F	—	—	—	—	—	—	—	—	—	—	—	—	—
1939	M	1	—	—	—	—	—	—	—	—	—	—	—	1
	F	2	—	—	—	—	—	—	—	—	—	—	—	2
1940	M	3	1	—	—	—	—	—	—	—	—	—	—	4
	F	1	—	—	—	—	—	—	—	—	—	—	—	1
1941	M	—	—	—	—	—	—	—	—	—	—	—	—	—
	F	—	—	—	—	—	—	1	—	—	—	—	—	1
1942	M	1	—	—	—	—	—	—	—	—	—	—	—	1
	F	2	1	—	—	1	—	—	—	—	—	—	—	4
1943	M	1	—	—	—	—	—	—	—	—	—	—	—	1
	F	—	—	—	—	—	—	—	—	—	—	—	—	—
1944	M	5	—	—	—	—	—	—	—	—	—	1	—	6
	F	3	—	—	—	—	—	—	—	—	—	—	—	3
1945	M	3	—	—	—	—	—	—	—	—	—	—	—	3
	F	1	—	—	—	—	—	—	—	—	—	—	—	1
1946	M	2	—	1	—	—	—	—	—	—	—	—	—	3
	F	1	—	—	—	—	—	—	—	—	—	—	—	1
1947	M	3	—	—	—	—	—	—	—	—	—	—	1	4
	F	—	—	—	—	—	—	—	—	—	—	—	—	—
Total	M	19	1	1	—	—	—	—	—	—	—	1	1	23
	F	10	1	—	—	1	—	1	—	—	—	—	—	13

Infantile tetanus is, therefore, almost entirely a disease of the neonatal period, and even at this age, as at other ages, affects males much more than females.

Fatality.—In the absence of comprehensive morbidity statistics it is difficult to estimate the fatality (case mortality) rate of tetanus in the civilian population. Except in infancy, and if treatment is prompt, it is possible that about 40–50% of cases will recover (Press, 1948). Before antitoxic serum became available for treatment the recovery rate was only about 15% (Bruce, 1920).

Geographical Incidence

Table IV gives numbers of deaths and death rates in the geographical regions of England and Wales during 1938–48, distinguishing the sexes during the periods 1938–41 and 1947–8. It has been noted in France that the death rates from tetanus have for many years been consistently higher in two or three of the departments into which the country is divided for purposes of civil administration. A similar tendency is revealed by the regional analysis in Table IV, which indicates that between 1938 and 1948 the highest rates in England and Wales were consistently recorded in the East and South-west regions, the difference between the rates in these regions and the others being more than would be likely to have arisen by chance.

A possible explanation for the high rates in the East and South-west regions is that a large proportion of the popu-

lation in those areas live in rural districts and are engaged in agriculture. Horses and other farm animals undoubtedly excrete *Clostridium tetani*, and a wound suffered by a person living in a country area is more likely to be contaminated by dirt or soil infected with tetanus bacilli than a wound in a town dweller. This explanation is supported by Table V, which compares the death rates from tetanus in 1946–8 among residents of Greater London, county boroughs, other urban districts, and rural districts. In each sex the death rates in the rural districts were about three times as high as in Greater London and the large towns, and more than half as high again as in the smaller towns.

TABLE IV.—*Deaths From Tetanus and Mean Annual Death Rates Per Million Living in Geographical Regions, England and Wales, 1938–48*

	1938–41				1947–8				1938–48	
	Males		Females		Males		Females		Persons	
	No	Rate	No.	Rate	No	Rate	No.	Rate	No.	Rate
England and Wales	310	4·1	78	0·9	97	2·4	43	1·0	938	2·1
Greater London	41	2·9	6	0·4	10	1·3	4	0·5	111	1·4
Remainder of South-east	63	5·9	14	1·1	22	3·8	12	1·8	199	3·1
North I	10	2·5	4	0·9	6	2·8	2	0·9	43	1·9
North II	15	6·2	2	0·7	4	3·2	2	1·5	47	3·4
North III	13	2·0	5	0·7	5	1·5	1	0·3	38	1·0
North IV	29	2·6	14	1·1	9	1·6	4	0·6	87	1·3
Midland I	39	4·3	6	0·6	17	3·4	2	0·4	104	1·9
Midland II	23	4·9	5	0·9	4	1·6	5	1·8	59	2·1
East	29	8·3	6	1·5	10	5·4	6	3·0	103	5·1
South-west	32	8·0	10	2·1	7	3·4	5	2·1	92	3·8
Wales I	13	3·7	5	1·3	1	0·6	—	—	36	1·8
Wales II	3	2·2	1	0·6	2	3·0	—	—	19	2·4

Note.—For the constitution of the geographical regions see the Registrar-General's Statistical Review for any recent year.

TABLE V.—*Deaths From Tetanus and Mean Annual Death Rates Per Million Living. Density Aggregates of England and Wales, 1946–8*

	Males		Females		Persons	
	No.	Rate	No.	Rate	No.	Rate
England and Wales	138	6·9	65	2·9	203	4·8
Greater London	16	4·2	6	1·4	22	2·7
County boroughs	26	4·3	14	2·1	40	3·1
Other urban districts	47	7·5	27	3·8	74	5·5
Rural districts	49	13·0	18	4·5	67	8·6

Occupational Mortality.—It seems probable, in view of the relatively high mortality of tetanus in rural districts, that persons engaged in farming and related occupations are exposed to the greatest risk. This, however, cannot at present be confirmed from the national mortality statistics, because the relationship between tetanus and occupation has not so far been studied in the Registrar-General's Occupational Mortality Supplements.

Prevention

Two forms of artificial immunization can be used in the prevention of tetanus. Each has been tested on a large scale in one of the two world wars.

Passive Immunization.—That an injection of antitoxic serum given soon after the time of wounding would prevent tetanus was clearly demonstrated in the 1914–18 war. In September, 1914, the tetanus rate among wounded British soldiers was 9 per 1,000. Routine injection of antitetanus serum was started in October, 1914, and by the end of the year the rate had fallen to 1.4 per 1,000 (Bruce, 1920).

Active Immunization.—Proof of the efficacy of this form of prophylaxis against tetanus also rests on military experience. A formolized toxoid for the production of active human immunity against tetanus was first produced in France about 1931. Active immunization of the French Army with this toxoid was begun in 1936, and by 1939 600,000 French soldiers had received two injections of toxoid at approximately a year's interval, which was then thought sufficient to give a solid immunity against tetanus. Unfortunately, owing to the French collapse in 1940, it proved impossible to preserve the records of this pioneer experiment of military medicine and to determine its results (Ramon, 1950).

Active immunization against tetanus with a formolized toxoid was begun in the British Army in 1939 and continued throughout the war. British wounded were, however, also given injections of antitoxin as soon after the injury as possible. This combined active and passive immunization was extremely successful, the number of cases of tetanus being reduced to insignificant proportions, the incidence among British troops being no more than 1/25 what it was in the 1914–18 war (Boyd, 1946).

The armed Forces of the United States during the last war relied entirely upon active immunization to prevent tetanus. At the time of wounding, or as soon after as possible, a boosting dose of toxoid was given, and not, as in the British Army, an injection of antitoxin. The results of this active immunization used alone proved to be as good as those of combined active and passive immunization used by the British, and the number of cases of tetanus among the American armed Forces was negligible (Long and Sartwell, 1947).

Experience in the British and U.S. Armies during the last war showed, moreover, that tetanus toxoid, unlike some other antigens, could be given subcutaneously without producing a local reaction and that it rarely caused general reactions. Active immunization with tetanus toxoid is therefore a practically trouble-free procedure.

Only one of the two available methods of artificial immunization against tetanus has hitherto been used in this country on any considerable scale among civilians.

Passive Immunization of Civilians

The injection of antitoxic serum for the prevention of tetanus became established as a routine in civilian hospitals and also to a certain extent in civilian general practice all over the world before the end of the 1914–18 war. It is still the only prophylaxis against tetanus in general use among civilians in this country.

The mortality data given above show, however, that this procedure is either not completely effective or is not applied widely enough among civilians. Moreover, civil and military experience shows that in susceptible persons tetanus antitoxin, like other antisera, is occasionally a cause of severe hypersensitivity reactions, some of which, unfortunately, prove fatal. More often antitoxin causes the less severe but temporarily disabling sensitivity reaction comprising an irritating skin rash and joint effusions known as "serum sickness." In view of the frequency of these complications many doctors, before deciding whether or not to give prophylactic injections of antitoxic serum, attempt to discriminate between wounds which may be more or less likely to cause tetanus.

It seems, however, to be the specific contamination which determines subsequent tetanus rather than the extent or depth of the wound, and tetanus has

occasionally been reported after trivial abrasions of a sort which would not be likely to receive medical or any other treatment. In general medical practice it must in fact often be extremely difficult to balance the risk of tetanus arising from a trivial wound against the risk of a serious hypersensitivity reaction to antitoxin. In hospital practice such decisions hardly ever have to be made, because only wounds of considerable severity are ordinarily presented for treatment, and for these antitoxin is quite rightly given as a routine.

Active Immunization of Civilians

Military experience clearly suggests that civilian tetanus might be almost completely prevented by means of active immunization with toxoid. Widespread adoption of this relatively trouble-free type of inoculation against tetanus would, moreover, free the doctor in general practice from the onus of making the difficult decisions which he now often has to make about the prophylactic use of tetanus antiserum in dealing with trivial injuries. It should be remembered, however, that the administration of routine pre-injury active immunization instead of, as at present, an *ad hoc* post-injury passive immunization against tetanus is likely for obvious reasons to be much more difficult among civilians than among soldiers.

The present incidence and mortality of tetanus are so low that in order to bring them to the vanishing-point—and anything less could hardly be regarded as worth while—it would be necessary to initiate and maintain active immunity in the whole population. Further, in order to prevent tetanus during the first month of life, when, as has been shown above, the risk is particularly great, special measures to ensure that the active immunity of expectant mothers was raised to the highest possible level during pregnancy would need to be taken.

The method of active immunization against tetanus now advocated (Parish, 1948) is to inject three doses of toxoid. The interval between the first and second injections is six weeks, and the third injection is given after a further interval of six to twelve months. To give such a series of injections to every man, woman, and child in the country would clearly be an expensive undertaking and extremely difficult to organize, especially on a voluntary basis, which is the only one that can be seriously considered.

Failing universal active immunization against tetanus, which can hardly be regarded as a practical proposition for health departments or for the medical profession at the present time, there remains to be considered the active immunization of population groups selected by age, place of residence, or occupation.

The active immunization of a selected age group of the population has been attempted in France, where since 1940 it has been obligatory by law for tetanus toxoid to be given at the same time as immunization against diphtheria—at present, before the age of 18 months (Ramon, 1950). No figures are available, however, to show the extent to which this obligatory active immunization against tetanus is actually done, and the published rates do not yet show that tetanus has substantially declined as a cause of death among French children in the last few years.

Serious consideration has also been given in the United States to the active immunization with toxoid of selected population groups. In one review of tetanus in America (Press, 1948) it was noted that nearly one-half the reported cases of the disease followed injuries which were so trivial as to go untreated or undetected, and it was estimated that if the passive form of tetanus prophylaxis at present advocated—that is, immunization with antitoxin after injury—were to be conscientiously performed nearly one-third of the total population would at some time during life receive an injection of antitoxin. The high incidence of sensitization to serum proteins likely to result might be regarded as an important argument in favour of active immunization as an alternative form of prophylaxis, at least in children and in those adults whose occupation exposes them to more than the average risk of accident. In another review (Long, 1948), after an analysis of data showing that in America children from 5 to 14 years run the greatest risk of tetanus, the conclusion reached was that, although active immunization with toxoid is warranted for children and for those with special occupational hazards, it cannot at present be advocated for the United States population as a whole.

Active immunization of the whole population against tetanus has recently been advocated as a long-term policy in Denmark, civilians working with earth—that is, farmers, gardeners, and navvies—together with patients having chronic ulcers, being regarded as special groups deserving immediate attention (Lassen, 1949).

In this country, in view of the relatively high death rates from tetanus among children from 5 to 14 years of age, it might at present be reasonable to offer parents active immunization against tetanus when they are being asked to agree to the "boosting" inoculation against diphtheria at the time of entry to school—that is, at about 5 years of age. This ought not to present any insuperable administrative difficulty, and the active immunization of children of this age group might be specially urged in rural districts where the local population seems to run a greater risk from tetanus than elsewhere.

Until further data are available it is impossible to consider whether active immunization against tetanus should be advocated as a protection against special risks in certain occupations.

Summary and Conclusions

A review of the mortality statistics of tetanus among civilians in England and Wales during 1927–48 shows that during this period mortality in each sex was highest during infancy and childhood, lowest during the middle years of life, and rose again after the age of 50, especially among males.

In 1946–8 there was a considerable decline in the mortality of males from tetanus, and a much smaller decline among females.

Tetanus male death rates at all ages are much higher than the corresponding female rates.

Fatal infantile tetanus was, and is, almost entirely a disease of the neonatal period.

Between 1938 and 1948 the highest death rates from tetanus were consistently recorded in the East and South-west regions of the country. It is unlikely that these higher rates were due to chance.

Death rates from tetanus were higher among the population of rural districts than in London or in the large and small towns.

The outstanding success of active immunization against tetanus in the military experience of the last war is held to justify a careful consideration of the application of this form of prophylaxis among the civilian population in peacetime.

Active immunization of the whole civilian population against tetanus in peacetime is rejected as impracticable, but it is suggested that the active immunization of children at about the age of entry to school would be both practicable and justified, especially in rural districts.

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SPONTANEOUS INTRAPERITONEAL RUPTURE OF THE BLADDER IN THE PUERPERIUM

BY

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In most cases in which the bladder is ruptured, trauma due to a penetrating body from without or to a bony fragment from within is responsible, and the rupture is usually extraperitoneal. Most instances of intraperitoneal rupture are due to the concussion of a blow at a time when the bladder is distended, and it is commonly the alcoholic who is the victim of this disaster. Spontaneous rupture occurs with relative rarity, and Stone (1931) could find only 40 cases in the literature. He found it to be due to disease of the bladder wall, inflammatory or malignant, or to obstruction at the bladder neck or urethra, leading to gross over-distension of the bladder. Paralytic lesions form a small percentage of this type. This spontaneous type of rupture may be extraperitoneal, though it is more often intraperitoneal, the former being associated with diseases of the bladder wall, whilst the latter most frequently occurs with an obstructive lesion.

In Stone's review the precipitating factor immediately responsible for the catastrophe was invariably a sudden increase in intra-abdominal pressure, due to such causes as attempted micturition, straining at stool, and sudden lifting of a heavy weight. On five occasions the distended bladder ruptured during labour and once during the manual expression of the placenta on the fifth day of the puerperium. Rupture has been reported by Sarkar (1944) and Mussgnug (1947) in association with retention of urine due to an incarcerated gravid uterus. Claye (1941) describes a fatal case of rupture of the bladder wall on the tenth day of the puerperium due to a neglected distension with overflow, though in his case the tears were not complete and there was no extravasation of urine.

The mortality rate in this catastrophe has always been very high, and Stone's investigations showed that before 1900 the rates for intraperitoneal and extraperitoneal spontaneous rupture were 92.3% and 50% respectively. After 1900 the rates were 45.4% and *nil* respectively.

The clinical picture varies considerably, and the extraperitoneal type, with its less acute symptoms, often does not reach the consultant until there are signs of extravasation of urine, with its concomitant infection. In the intraperitoneal type, however, after a period of retention of urine, a sudden increase in intra-abdominal pressure is followed by severe abdominal pain and collapse. The picture of "acute abdomen" with rigidity follows, though shifting dullness may also be elicited in many cases.

In most of the earlier cases treatment was unsatisfactory, as it was not realized that post-operative drainage of the bladder was essential. Since this has been carried out the results have steadily improved, and Stone maintains that repair of the rent in the bladder is unnecessary, so long as the peritoneal cavity is drained and a suprapubic cystotomy carried out.

Diagnosis of spontaneous rupture of the bladder is difficult unless there is a history of retention of urine, with an associated obstructive lesion. In the following case there was no suspicion of the true diagnosis until the peritoneal cavity was searched at laparotomy.

Case History

A married woman aged 36 had a normal delivery of her second child on September 25, 1950, after a labour lasting seven hours. Her doctor had to express the placenta, and she had a second-degree perineal tear, which was sutured. Her first child had been stillborn two and a half years before, following a severe pre-eclamptic toxaemia. During the puerperium the patient complained of abdominal discomfort, which was thought to be due to after-pains; but she was otherwise well, and her chart showed no rise of temperature. On the morning of the fifth day after delivery the midwife suggested that the time had come for her to spend a few hours a day lying on her abdomen lest her uterus should become retroverted. This injunction was obediently followed, and immediately the patient felt a severe pain in the upper abdomen and collapsed. She vomited once shortly afterwards.

I first saw her in consultation with the doctor a few hours later, when the above history was obtained. At this time her temperature was 97° F. (36.1° C.), the pulse rate was 106 and of fairly good volume, while she was sweating profusely. Her colour was good, however, and the diagnosis of pulmonary embolus, as suspected by the doctor, seemed improbable. The pain was localized to the upper abdomen, and on inspection the abdomen appeared generally distended, though this was most marked below the umbilicus. Palpation revealed a cystic swelling which filled the whole of the lower abdomen and rose to about two fingerbreadths above the level of the umbilicus. This was tender, but not as markedly so as the epigastrium and hypochondria. There was no rigidity, but the muscles had been stretched by the pregnancy and had not yet regained their tone, and the most outstanding feature was the pain felt when the pressure of the hand was released. The swelling in the abdomen was dull to percussion. A pelvic examination was not then carried out as it was obvious that the patient would have to be moved into hospital. A ruptured ovarian cyst was provisionally diagnosed, and arrangements were made for her transfer.

On arrival at hospital nearly two hours later, after an ambulance journey of 16 miles, she was immediately catheterized, 26 oz. (740 ml.) of rather dark-coloured urine being obtained. When she was seen immediately afterwards the clinical picture had changed. She looked more shocked than when first seen, with a cyanotic tinge about the lips, though the pulse rate was about the same, and the B.P. was 110/70. On examination, however, instead of the cystic lower abdominal swelling, there was now a

generalized distension of the abdomen, with dullness on percussion corresponding to that of an ascites instead of an ovarian cyst. In addition a fluid thrill could be elicited. Pain and tenderness were unabated, however, and laparotomy seemed imperative.

Half an hour later the patient was anaesthetized, though the induction was difficult owing to the vomiting of dark "coffee-ground" material. The stomach was emptied with a stomach-tube, after which there was less difficulty. A metal catheter was passed into the bladder and another 6 oz. (170 ml.) of clear urine obtained. On bimanual vaginal examination no pelvic abnormality could be found apart from the large involuting uterus. A fluid thrill was still clearly present, however.

The abdomen was opened by a midline subumbilical incision, and immediately a straw-coloured odourless fluid began to flow out. Six pints (3.4 litres) of this was removed with the sucker and the rest mopped out with gauze until a clear view of the abdominal contents could be obtained. The uterus was pale and normal in size for this stage of the puerperium, while the small bowel and omentum were also of normal appearance. Both ovaries and tubes were inspected and found to be normal. The upper abdomen was explored with a hand, and nothing abnormal was discovered. More by good fortune than design, the uterus was pushed backwards and the utero-vesical pouch examined, and there in the fundus of the bladder was a hole big enough to admit one or two fingers; its edges were necrotic and gangrenous.

The necrotic edges were cut away and the hole was repaired by continuous sutures in two layers. An assistant introduced a Malecot self-retaining catheter into the bladder, via the urethra, before the abdomen was closed, to safeguard against further injury to the sutured fundus. A little remaining fluid was mopped out of the peritoneal cavity, and the abdomen closed without drainage. The patient's general condition was not very good, and an intravenous saline drip transfusion was started and a Ryle's tube left in the stomach. A pint (570 ml.) of blood was transfused a few hours later. The bladder was allowed to drain into a Winchester bottle. Penicillin, 200,000 units, was given three-hourly.

The post-operative course was impaired at first by a troublesome cough with a purulent sputum, though there was only slight pyrexia. Some intestinal distension developed, but spontaneous passage of flatus occurred on the third day, when the drip was discontinued. The Ryle's tube had been removed the day after operation. An enema was now given, and flatus resulted. By the fifth day the patient was eating a light diet, and sulphamezathine, 0.5 g. four-hourly, was started. The catheter was removed on the ninth day, and micturition was immediately possible, though in small quantities at a time. Estimation of residual urine in the morning and evening showed 25 oz. (710 ml.) in the bladder at first, though this gradually diminished to a few ounces by the fourteenth day, when further catheterization was considered unnecessary. Ambulation had been allowed as soon as the catheter was removed. Sulphamezathine was continued until the residual urine had disappeared. The patient was discharged from hospital on the eighteenth post-operative day.

Comment

Spontaneous intraperitoneal rupture of the bladder in the puerperium is an extremely rare event, and no record of any other case can be found, except one in which manual expression of the placenta was being attempted on the fifth day. There is therefore little to be learnt from such an occurrence, though it may be pertinent here to make the following remarks: (1) Palpation of the involuting uterus is still an important part of the after-care of the puerperal patient. Delay in the descent of the fundus is often an indication that the bladder is not being emptied completely, and that residual urine is collecting. (2) Early ambulation is probably the best means of ensuring that a patient empties her bladder completely.

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AUREOMYCIN AND CHLORAMPHENICOL IN CHANCROID

BY

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Reports concerning the action of "aureomycin" and chloramphenicol on chancroid have been somewhat conflicting. Thus, Wetherbee *et al.* (1949), who tested streptomycin, aureomycin, and a number of other antibiotics *in vitro* against *Haemophilus ducreyi*, thought that aureomycin had only a transitory effect, and that of the drugs tested only streptomycin was likely to be of value for soft sore. Nell and Hill, quoted by Robinson (1950), likewise found the inhibitory effects of aureomycin inferior to penicillin, but stated that chloramphenicol was effective. Working on the human infection, however, Zheutlin and Robinson (1950) reported three clinical cases successfully treated with 2 g. of aureomycin daily for 7–14 days, while Greenblatt *et al.* (1950) recorded yet another case. On the other hand, the latter workers believe that 5–10 g. of chloramphenicol is necessary.

The present work was undertaken in Africa during 1949, on both experimental and clinical infections.

Experimental Infection

An intradermal inoculation of 0.05–0.1 ml. of fluid aspirated from chancroidal buboes was given either to the patients themselves or to other volunteers. If both the donor and the recipient are untreated a local pustule develops within 48–96 hours and proceeds to chancroidal ulceration. If the recipient is treated with effective drugs at the time of inoculation, or the donor before inoculation, no such reaction occurs. Three series of experiments have been described (Willcox, 1950a, 1950b, 1950c), referring respectively to (1) the auto-inoculation of the donors; (2) the hetero-inoculation of volunteers treated with material from untreated donors; and (3) the hetero-inoculation of volunteers with material taken from treated donors 24 hours and later after the beginning of treatment.

Chloramphenicol.—Bubo fluid from Case 1 (see below), proved virulent by injection into an untreated volunteer, was injected into the patient himself, who then received 250 mg. of chloramphenicol orally three times daily for three days. A local bump was evident at 48 hours and persisted until 120 hours, when it was needled but found not to contain pus. Bubo fluid from this donor was also inoculated into five other men 24–48 hours after the treatment had begun, and all failed to show a take, thus indicating that the fluid had lost its virulence. Four others, who received inoculations with

material of proved virulence taken from three untreated donors, were given between seven and twelve 250-mg. capsules of chloramphenicol orally over three to five days. None of these showed a take, although takes were observed in five out of six controls inoculated with the same material.

Aureomycin.—Case 3 was inoculated with his own bubo fluid, which produced three takes out of three in untreated controls, prior to treatment with 2 g. of aureomycin given orally over three days. The arm showed a local bump at 24–96 hours, at the end of which time it was needled but contained no pus. At seven days, however, an ulcer had formed, but it seemed that the ulceration was delayed by the use of the drug. Bubo fluid from this patient was inoculated into 13 others 24–120 hours after the onset of treatment; there was a take in only one (inoculated at 24 hours), and twelve showed no reaction. In addition hetero-inoculations, from four donors whose bubo fluid had produced 15 takes in 17 untreated controls, were made into ten persons, who were immediately given aureomycin orally, the dosage amounting to 500–1,250 mg. over two to four days. There was no take in any.

Clinical Infection

Three cases are reported—two treated with chloramphenicol and one treated with aureomycin.

Case 1.—A young male African negro presented with a fraenal soft sore, with a tender ripening left bubo of two weeks' duration. There was a history of sexual exposure seven days before the onset. Repeated dark-field examinations for *Treponema pallidum* were negative, as was the serum test for syphilis. The Dmelcos skin test for chancroid was, however, positive. He was then treated with 250 mg. of chloramphenicol orally three times daily for three days. The sore was noted to be healing by the second day, by which time the inguinal gland was no longer tender. The sore had completely healed by the fifth day, but the gland required aspiration.

Case 2.—A young male native of Southern Rhodesia attended with a rosette of preputial soft sores of 18 days' duration, but without enlargement of the inguinal glands. Three consecutive daily dark-field examinations were negative for *T. pallidum*, but the serum Wassermann reaction was positive, as was the Dmelcos skin test. He was considered to be a latent syphilitic with superadded chancroid. Two days before treatment this patient had acted as a control in another series of experiments and exhibited an arm pustule in addition. He was given a total of 2,000 mg. of chloramphenicol orally in eight-hourly doses over three days, and by the end of this time the penile sores had entirely healed, but the arm pustule proceeded quietly to a non-angry ulceration before ultimately healing without other measures.

Case 3.—A young male negro from Portuguese East Africa had multiple soft sores of the prepuce, with bilateral fluctuant inguinal buboes, of five days' duration. There had been an exposure two days before this. Repeated dark-field examinations were negative for *T. pallidum*; the serum Wassermann reaction was negative, but the Dmelcos skin test was positive. He was given a total of 2,000 mg. of aureocycin orally over three days. The penile sores healed within four days, but the right bubo required aspiration (15 ml. of avirulent fluid being removed on the fourth day), while the left leaked spontaneously. All was normal by the eighth day.

Discussion

In European and American clinics drugs which have no action on *T. pallidum*—for example, the sulphonamides—together with a proper follow-up, are rightly preferred for the treatment of chancroid, lest an early concomitant syphilitic infection be masked. Both aureomycin (O'Leary *et al.*, 1948; Irgang and Alexander, 1949; Willcox, 1949) and chloramphenicol (Romansky *et al.*, 1949; Willcox, 1950d), like penicillin, have been shown to have a healing action upon the lesions of early syphilis, as has terramycin and also, to some extent, streptomycin (Willcox, 1950e). Thus in well-developed communities, although penicillin, aureomycin, and chloramphenicol are all effective against soft sore, their antisyphilitic action limits their use to those cases in which resistance to sulphonamides is evident, or when phagedaena occurs and the risk of masked syphilis is small against that of threatened loss of part or all of the member.

In Africa, however, the conditions are somewhat different, especially in facilities for accurate diagnosis and follow-up, which are often virtually non-existent. It is therefore not unreasonable to treat all cases of penile sore in the African with the routine employed for syphilis, provided that the drug given is effective also against chancroid. Penicillin is very suitable, and many workers—for example, Moore (1949)—consider that its place in the treatment of syphilis is still secure. It seems likely that the single injection of 2,400,000 units of procaine penicillin with 2% of aluminium monostearate, which gives results in early syphilis almost as good as those obtained with eight daily injections of 600,000 units (Bauer *et al.*, 1950), and is at the same time reasonably effective against soft sore (Willcox, 1950f), is the optimum routine treatment for genital sores under African conditions.

Although the oral antibiotics have all the medical drawbacks of penicillin in the treatment of chancroid, the fact that they are given orally may prove a blessing in the bush, where administration may be effected, under supervision, by unskilled persons. The same fact is viewed with concern by physicians in more civilized countries, who rightly fear indiscriminate and improper treatment by quacks, or by the patients themselves, without even the certainty, as with penicillin, that the patient has actually received the dose prescribed.

Summary

Experiments in which volunteers were inoculated with chancroidal bubo fluid indicated that both aureomycin and chloramphenicol were capable of preventing the experimental infection in man, and also in rendering the bubo fluid avirulent.

Two clinical cases of soft sore were successfully treated with chloramphenicol and one with aureomycin, although fluctuant buboes still required aspiration.

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Medical Memoranda

Stab Wound of the Heart

Stab wounds of the heart seem to be a rarity in Great Britain. I have found only one reported case of surgical repair (Gissane and Schulenburg, 1937). The condition, however, is not uncommon in the U.S.A., especially among coloured people. Several large series of surgically treated cases have been reported, with an overall mortality of less than 50%, while in some smaller series the mortality rate has been much less. If a patient lives to reach hospital, therefore, the outlook is remarkably good. This is rather contrary to what one might imagine. The following case is reported in order to draw attention to the good results of treatment.

Case Report

A man aged 54 was admitted to hospital at 6.25 a.m. on October 24, 1949, having attempted suicide about an hour previously by stabbing himself in the chest with a pair of scissors. He was seen on admission by Dr. E. Keen.

On examination he was restless and irrational, and cyanotic. When he was supine the external jugular veins were considerably distended, but when sitting up this partially disappeared. The systolic blood pressure was 50; the diastolic was not recordable. The pulse rate was 95. The heart sounds on auscultation were faint. There were three puncture wounds over the praecordium to the left of the sternum. An intravenous drip was begun. Approximately 10 oz. (284 ml.) of blood was given before his arrival in the theatre at 8.30 a.m., when his condition had deteriorated markedly. The cyanosis was very noticeable, the radial pulse was not palpable, and the blood pressure was not recordable.

An attempt was made to aspirate the pericardium with a large-bore needle through both the subcostal approach and the fourth left interspace. Nothing, however, was obtained. A light general anaesthetic was then begun by Dr. J. Black. Thoracotomy was performed through the fourth left intercostal space from the axilla to the right border of the sternum. The fourth and fifth costal cartilages were divided adjacent to the sternum. A rib spreader was inserted. The pericardium was seen to be tense and bulging, the cardiac pulsation being just palpable. A small incision was made in the pericardium and enlarged downwards, forwards, and medially with scissors. A considerable quantity of blood clot extruded spontaneously. The patient's condition improved dramatically with relief of the tamponade. Copious venous bleeding then occurred.

The heart was palpated and a wound in the anterior surface of the right ventricle found. This admitted the terminal phalanx of the left index finger, being ¾ in. (2.2 cm.) in length. The insertion of the finger controlled the bleeding. As exposure was not good the skin incision was carried vertically downwards in the midline and the incision of the pericardium enlarged to give adequate exposure. A stay suture was inserted through the ventricular wall in the line of the wound and a deep suture passed under the finger as the latter was withdrawn. This suture was then tied, but, unfortunately, the friability of cardiac muscle was not appreciated and it cut out, converting a simple linear wound into a T-shaped rent. Torrential bleeding occurred. Three further sutures were rapidly inserted across the wound and tied. These went right through the wall and included endocardium. Most of the bleeding was now controlled, and complete haemostasis was finally obtained by the insertion of four further sutures through the muscle. Catgut was used for all sutures. The pericardium was then partially closed, the pleural cavity evacuated of blood by suction, and the chest closed without drainage, after expansion of the lung. During operation 3 pints (1.7 litres) of blood was transfused under pressure.

On the evening of October 25 the patient became cyanotic and dyspnoeic. Examination revealed collapse of the left lower lobe. Bronchoscopy was performed under curare–thiopentone anaesthesia and a considerable quantity of mucus aspirated through the left main bronchus and lower-lobe bronchus. An immediate improvement in air entry was observed, and post-operatively his condition was much improved and remained satisfactory until October 28, when a further collapse occurred in the left lower lobe. This responded to conservative measures—breathing exercises, penicillin, and sulphonamides. He was allowed up on November 15 and discharged on December 5. An E.C.G. on October 29 revealed no abnormality. When seen on February 6, 1950, he had apparently made a complete recovery.

Comment

The effects of heart wounds are in the main due to cardiac tamponade or exsanguination—the former when the pericardium is intact, the latter when a communication of sufficient size to allow free drainage exists between the pericardial and pleural cavities. In the above case the classical symptoms of tamponade were all present—namely, increased venous pressure giving rise to visibly distended veins and cyanosis, a fall in arterial pressure, and heart sounds which were faint and difficult to hear.

Blalock and Ravitch (1943) recommended conservative treatment, giving intravenous transfusions in an attempt to raise the venous pressure and overcome the tamponade. The fact that the external jugular veins became partially collapsed on sitting up suggests that the increased venous pressure in this position was overcoming the tamponade. An intravenous drip, however, of 10 oz. of blood pre-operatively had no effect in improving the circulation; bigger quantities may have done so, but I doubt this because of the free communication between the right ventricle and the pericardium. Aspiration is also advocated as a means of lessening the tamponade. In the above case, however, the clotting of the blood within the pericardium rendered this measure valueless.

Most authors recommend surgical approach and suture of the wounds. A variety of incisions have been employed, but that used in the above case is probably the easiest and quickest to make and seemed to give an adequate exposure. To control the bleeding Beck (1942) recommends a finger on the wound, but not in it, as the latter is apt to cause further tearing of the myocardium. The simple expedient, however, of plugging the hole with the finger proved of considerable value. The usual suture material recommended (Elkin, 1941; Beck, 1942) is fine silk. The use of catgut, however, had no apparent disadvantage, and was possibly advantageous in view of the fact that some of the initial sutures penetrated endocardium. An important point in suturing is to realize the friability of cardiac muscle. Failure to do so nearly caused a disaster. The pericardium was left partially unsutured in order to allow drainage into the pleural cavity of any further bleeding and prevent the recurrence of tamponade.

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Chordoma as a Cause of Obstetric Disproportion

Ganglion neuromata in the pelvis complicating pregnancy and labour have been reported on several occasions (Law, 1913, 1922; Strassmann, 1913–14; Sippel, 1923; Turunen, 1940; Foster, Berman, and Compton, 1942), but a search of the literature has failed to reveal a recorded case of dystocia caused by a chordoma. It is therefore considered that the following case should be recorded.

Case Report

A primipara aged 36 was seen at the antenatal clinic at the 36th week of pregnancy. She felt well except for pain in the region of the left hip which radiated down the back of the thigh, and numbness of the left foot. She had had the pain in varying degrees for the past eight years, and on three occasions had almost lost the power of the left leg. Sometimes "pins and needles" were felt. She also noticed that flexion of the spine aggravated the pain, as also did the pregnancy.

On examination she appeared to be a healthy woman. Examination of the central nervous system showed reflexes, power, and sensation to be normal and equal on both sides. There was a suggestion of wasting of the left leg and buttock, noticeable on inspection, but not sufficient to be confirmed by measurement. Movements of the spine were limited, but this was thought to be due to the pregnancy. A foetus the size of a 36-weeks pregnancy was found to be presenting as a vertex, but free above the brim.

Vaginal examination revealed a very tender soft cystic tumour fixed to the left side of the sacral promontory; the lower border was definable—the upper border could not be reached. It appeared to be just below the level of the promontory, and was difficult to distinguish from it. The distance from the front of the tumour to the lower border of the symphysis pubis was clinically about 3¾ in. (9.8 cm.). The pelvis was otherwise normal. On rectal examination the tumour, which lay behind the rectum, was more obvious, and the vaginal findings were confirmed. *X*-ray pelvimetry revealed a normal pelvis, but in the antero-posterior view an erosion of the left side of the body of the first sacral vertebra could be seen.

A week later the patient was admitted to hospital, as the pain was much worse. It continued to increase, and the pelvic tumour appeared to fluctuate in size, the palpable part varying in size between a small cherry and a large plum. No definite diagnosis was made at this time regarding the nature of the tumour, but it was felt that ganglion neuroma was a possibility.

At 38 weeks' maturity, because the pain was very severe and the foetal head could not be made to engage, it was decided that a lower uterine section should be done and an attempt be made to remove the tumour at the same time. Pre-operative intravenous pyelography showed both ureters to be in a normal position. Accordingly, after a healthy infant had been delivered and the uterine incision closed, the tumour was examined. It was found to be coming through the first sacral vertebral foramen on the left side. The pelvic portion was the size of a plum, cystic, vascular, and with a well-defined lower border which seemed to be attached to the first sacral nerve root. The tumour did not extend up into the abdomen, and, because of the large uterus, access to it was not easy. However, the peritoneum was dissected off the front of the tumour, and, as the attachments made its removal impracticable at this time, a piece was taken for biopsy. There was a fair amount of bleeding, which was controlled by pressure.

After operation the obstetric progress was normal. The sciatic pain disappeared for the first 10 days, but then reappeared. Examination of the central nervous system on the 16th day revealed an absent left ankle-jerk and gross limitation of flexion of the lumbar spine. Flexion of the right hip was 90 degrees and of the left hip 60 degrees.

The patient was transferred to the care of the neurosurgeons, and two months later, after a cisternal myelography which showed a complete block at the level of the fourth lumbar vertebra, Mr. Eric Paterson operated through a midline incision over the lower lumbar and upper sacral segments. There was a large protrusion of tumour through an aperture in the posterior surface of the sacrum just to the left of the midline and centred at the level of the second sacral vertebra. It extended through the anterior surface of the sacrum to expand into the large mass felt per vaginam. Above, opposite the fifth lumbar vertebra, was a similar protrusion on the right postero-lateral aspect of the theca, which was narrowed by the masses of tumour growth at and below this level and distorted into an S curve. The tumour was extremely vascular and very soft in consistence; its accessible portions were scraped away, but complete removal was obviously impossible.

Dr. A. Dick reported on the specimen as follows: "Histological examination of the material shows the structure of a chordoma with numerous areas of haemorrhage."

A year later the patient was symptom-free apart from some generalized rheumatism, though there was probably a local recurrence of the tumour in the pelvis; the left sacral ala was obscured by thickening, and the diagonal conjugate reduced to 3¼ in. (8.2 cm.).

Comment

The interest of this case seems to be partly in the rarity of such a tumour as a cause of dystocia, and partly on account of the fact that, although the symptoms had lasted for eight years and the patient has been thoroughly investigated several times for sciatica, the presence of the tumour was not demonstrated until the routine vaginal examination at the 36th week of pregnancy. The correlation of the tumour with the neurological symptoms then became evident, and one wonders if its growth had been accelerated by pregnancy. The first tentative diagnosis was a ganglion neuroma—fibroma, lipoma, and sarcoma being also regarded as possible: it was only at operation that the spinal origin of the tumour was discovered.

We would like to thank Mr. Eric Paterson for his help and co-operation with the case; and Dr. D. Mackay Hart and Dr. R. G. H. Cunningham for permission to publish.

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Since last June a special anti-tuberculosis centre, established by W.H.O., has been at work in Istanbul (Turkey) training medical men and health workers in modern methods; and a permanent building for it was opened on February 17, providing the occasion for a review of its work. In eight months the staff has given courses to nearly 300 doctors and nurses, tuberculin-tested 8,000 people, and given 3,000 vaccinations, while 10,000 *x*-ray examinations have been made. The staff consists only of a French specialist, an English technician, and a French nurse. Tuberculosis is estimated to cause 40,000 deaths annually in Turkey. Another W.H.O. centre has already been established in New Delhi, and others are planned for Thailand, Burma, Pakistan, Ceylon, and El Salvador.

Reviews

TEXTBOOK OF MEDICINE

A Textbook of the Practice of Medicine. By Various Authors. Edited by Frederick W. Price, F.R.S.(Ed.), M.D., C.M.(Ed.), F.R.C.P.(Lond.), Hon.M.D.(Belf.). Eighth edition. Oxford Medical Publications. (Pp. 2,076. £2 5s.) London: Geoffrey Cumberlege (Oxford University Press). 1950.

For years "Price" has been regarded as a standard textbook, and its successive editions, like milestones, have marked the majestic progress of medicine. Its contributors have always been men of distinction, for whom Collier set an early standard of excellence with his suberb chapter on diseases of the nervous system. Perhaps more than any other British textbook of medicine it is regarded abroad as representing the medical practice of this country. It is natural therefore that we should be sensitive about our ambassador's appearance and views.

The eighth edition contains much new material and has several new contributors. It is 42 pages longer than its predecessor, so that the well-marked middle-aged spread of the seventh edition remains troublesome, making the volume unsightly and clumsy. It would be more comely and manageable were it taller and thinner. The binding is of poor quality and the printing indifferent, but the cost is very moderate for a book of this size. In the copy sent for review pp. 705 to 736 inclusive were missing. The work seems to have suffered even more than other books published just now in this country from the length of time it has taken in the press, so that many recent advances of medicine find little or no mention in it.

Much of the contents—particularly the description of disease—is admirable. The weakness of the work lies in its paragraphs on treatment, which occupy a not inconsiderable portion of the book. Too many therapeutic measures are often mentioned, leaving the reader in doubt about which to choose; accounts of remedies which have had their day and been found wanting are frequently perpetuated; and useful measures are described in insufficient detail. These points are well exemplified in the treatment of pneumonia, p. 1296, and in that of urticaria: ". . . mild purgatives and the administration of intestinal antiseptics, such as salol, ichthammol, creosote and calomel, can be recommended. Some patients improve on tonic drugs, such as iron, arsenic and quinine. Antihistamine drugs have proved very useful in many cases; or ephedrine hydrochlor. gr. ½ t.d.s. may be tried." Sulphapyridine still crops up occasionally in this 1950 edition, though it has vanished even from the conservative pages of the 1948 *British Pharmacopoeia*. Vaccines are often recommended in circumstances in which their value is indeed doubtful, and butcher's meat is still banned in the management of hypertension, although "fish, poultry, game (not high)" are considered suitable. In the treatment of bronchiectasis there is no discussion of the indications for lobectomy, but creosote baths are fully considered. A long paragraph is devoted to the description of a compressed-air chamber for the alleviation of emphysema, but on the same page the controversial treatment of cor pulmonale is summarily dismissed in four lines, which, however, do not forget leeching. There is no discussion of the place of sympathectomy in hypertension, nor is there anywhere more than a passing mention of modern anticoagulants. But space is found for a nostalgic reference to the efficacy of sodium cacodylate in asthma.

A carping critic can always find material for a splenetic review in a medical work of 2,000 pages, however excellent it may be. Unfortunately this volume, which should be so good, provides such abundant scope for animadversions that the space allotted for its review is insufficient to chronicle more than a small fraction of them. The eighth edition of "Price" has increased in girth but not in stature.

D. M. DUNLOP.

RECENT OPHTHALMOLOGY

Recent Advances in Ophthalmology. By Sir Stewart Duke-Elder, K.C.V.O., M.A., D.Sc., LL.D.(St. And.), Ph.D.(Lond.), M.D., F.R.C.S., Hon. D.Sc.(Northwestern), F.R.C.S.(Ed.), F.A.C.S., and Allen J. B. Goldsmith, M.B., B.S.(Lond.), F.R.C.S. Fourth edition. (Pp. 372; 6 coloured plates and 133 text figures. £1 8s.) London: J. and A. Churchill. 1951.

The fourth edition of this book comes 17 years after the publication of the third and is a completely new book. Rather more than one-third of the text is devoted to the intraocular fluids and glaucoma, and includes discussions on the clinical significance of the blood–aqueous barrier, the work of the Zurich school on the cytology of the aqueous, the role of aqueous veins in drainage, and the practice and value of gonioscopy. In an equally extensive section the authors discuss infection by bacteria and viruses, and chemotherapy and the antibiotics. That an endocrine factor may be responsible for inflammation is indicated, though the authors appear to adhere to the older theory of infection in some modified form. The concluding three chapters are on the cornea and conjunctiva, cataract, and endocrine exophthalmos.

There is a judicious blend of the purely theoretical and the essentially practical aspects of ophthalmology, and in the fields selected by the authors their review is detailed and intensive. The historical matter included in the section on the antibiotics captures some of the early excitement caused by the therapeutic revolution still in progress. While no attempt has been made to cover the whole field of ophthalmology, significant developments during the period under review have all been noted. The clinician will be especially interested in the accounts of gonioscopy, biomicroscopy of the fundus, brucellosis, toxoplasmosis, the virus diseases, penicillin therapy, keratoconjunctivitis sicca, and rubella.

ARNOLD SORSBY.

HEALTH IN SCHOOL-CHILDREN

Handbook of Child Health. By Austin Furniss, L.R.C.P., L.R.C.S.(Ed.), L.D.S., D.P.H.(Univ. of Manchester). (Pp. 280. £1 5s.) London: Sylviro Publications, Ltd. 1950.

Dr. Austin Furniss has written a useful little book, though the title is misleading in the sense that he discusses only the child at school. The book is refreshing in its approach, for there is no section on the periodic examination of school-children. Instead the author broadly considers nutrition, growth, and diet before going on to discuss the special aspects of nursery schools and open-air schools. In the rest of the book he describes in detail the problems presented by the child who is handicapped, mentally and physically. He might

have included more about the child with juvenile rheumatism, with or without heart disease, and should have mentioned the pioneer "heart homes" such as West Wickham and the rheumatism supervisory scheme of the London County Council. This is, however, the only serious omission. Otherwise the author reviews most of the conditions with which the school doctor has to deal. It would have been interesting if he had included a chapter on the duties of a school nurse (though he mentions them in some sections) and his views on the part which the doctor can play in the individual school in conjunction with the teaching staff. "B.C.B. vaccination" on page 83 is an unfortunate misprint.

It is interesting to note the author's conclusion that the three biggest problems of the school health service are infestation, dental disease, and mental retardation, but he is perhaps pessimistic in stating that little can be done about the last. There is surely scope for a bold constructive policy of help for parents of such children. Students working for the D.C.H. or D.P.H. will find this a helpful volume.

ALAN MONCRIEFF.

BIOLOGY FOR THE CITIZEN

Biology: the Human Approach. By Claude A. Villee. (Pp. 580; 250 figures. £1 5s.) Philadelphia and London: W. B. Saunders Company. 1950.

In common with so many modern American textbooks intended to provide a general first-year university education in biology, that of Villee makes man the centre of interest. It is widely agreed that such human biology is the kind of biology which the enlightened citizen should know first and foremost, for it most easily captures and holds the ordinary student's interest and need not entail any sacrifice of basic scientific principles.

Villee has made the core of his book an account of human physiology. He has done this clearly and far from superficially. To this core he has attached a rather thin comparative treatment of plants and animals, linked to the human physiology mainly by the notion of an evolutionary scale of beings. Evolution is indeed, and rightly so, the guiding principle of the whole book, and the author concludes with a stiff section on formal genetics and an unusually full and well-balanced discussion of the theory of evolution and the evidence on which it is based. Such an evolutionary emphasis, admirable in itself, shows also considerable strength of purpose in an American author, since the American educational scene is not entirely favourable to the teaching of evolution.

The author's definite view of what human biology should be stimulates some questioning of its adequacy. In spite of the emphasis on physiology and evolution, it can be argued that the picture of the organic world that the author paints is not really a living one. The reason is that the dynamic relations of organisms to each other and to their physical environment appear little more than incidentally. Yet these relations are surely of vital importance to biological science, including evolutionary theory; and, since man is bound by them, they are no less important to the educated citizen, whose survival depends on them. The relevance to the practice of medicine of a public well grounded in human physiology can be granted. But the emphasis in this book is perhaps too much on the human body, for it has meant neglect of other aspects of biology of equal importance to human beings and of considerably greater biological generality. After reading the section on human diet one might say, though unfairly, that the emphasis is too much on the American body, for this section is devoted almost exclusively to a warning against over-eating.

Such questions of content are too much a matter of opinion to be made a subject of criticism, though they are an important subject for discussion. But there is a real criticism to be made. The book suffers here and there from that curse of so much elementary biology—theoretical feebleness. It is high time that protest was made against such carelessness as the definition of the principle of organic evolution in such a way as to apply only to the lineages of present-day organisms and only to the transition from simple to complex. Then there is that inevitable list of characteristics all of which are supposed to be possessed by all known living things. There are said to be six of them, and to justify three of these—reproduction, movement, and growth—would strain ingenuity to breaking-point. Villee is of course doing no worse, and often a good deal better, than most textbook writers. These half-baked generalizations drift from one textbook to another. Could not the new human biology break this bad old tradition?

M. ABERCROMBIE.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

Genetics in Ophthalmology. By A. Sorsby, M.D., F.R.C.S. (Pp. 251. 42s.) London: Butterworth. 1951.

A Dictionary of Biology. By M. Abercrombie and others. (Pp. 246. 2s.) Harmondsworth: Penguin Books. 1951.

Science News 19. Edited by J. L. Crammer. (Pp. 142. 1s. 6d.) Harmondsworth: Penguin Books 1951.

Malignant Disease of the Female Genital Tract. By S. Way, M.R.C.O.G. (Pp. 279. 24s.) London: J. and A. Churchill. 1951

Recent Progress in Psychiatry. Edited by G. W. T. H. Fleming. Vol. 2. *The Journal of Mental Science.* (Pp. 711. 50s.) London: J. and A. Churchill. 1950.

Experimental Physiology for Medical Students. By D. T. Harris, M.D., D.Sc., F.Inst.P., and others. 5th ed. (Pp. 305. 21s.) London: J. and A. Churchill. 1951.

Stress. By H. Selye, M.D., Ph.D., D.Sc., F.R.S.(Can.). (Pp. 1,025. No price.) Montreal: Acta 1950.

The Meaning and Practice of Psychotherapy. By V. E. Fisher, Ph.D. (Pp. 411. 37s. 6d.) New York: Macmillan Company. 1950.

Transactions of Conferences of the Josiah Macy, jun., Foundation. *Renal Function.* Edited by S. E. Bradley. (Pp. 172. $2.50.) *Metabolic Interrelations.* Edited by E. C. Reifenstein, jun., M.D. (Pp. 279. $3.95.) *Blood Clotting and Allied Problems.* Edited by J. E. Flynn. (Pp. 224. $3.) *Biological Antioxidants.* Edited by C. G. Mackenzie. (Pp. 181. $3.25.) *Cybernetics.* Edited by H. von Foerster. (Pp. 209. $3.50.) *Liver Injury.* Edited by F. W. Hoffbauer, M.D. (Pp. 164. $1.60.) *Problems of Aging.* Edited by N. W. Shock. (Pp. 258. $3.75.) New York: Josiah Macy, jun., Foundation. 1950.

Techniques et Thérapeutiques en Pneumologie. Edited by P. Bourgeois. (Pp. 365. 1,000 francs.) Paris: L'Expansion Scientifique Française. 1950.

Studien über die Morphogenese des Plattenepithelkarzinoms der Portio Vaginalis Uteri. By E. Glatthaar. (Pp. 84. 8 Swiss francs.) Basle: S. Karger. 1950.

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REMUNERATION OF GENERAL PRACTITIONERS

When the Spens Committee was considering the remuneration of general practitioners in the N.H.S. it was much concerned to see that the financial rewards of general practitioners should be such as to attract into its ranks men of first-rate ability. In the past there has always been in general practice a steady leavening of the average with men of more than usual ability. It is true that it was not necessarily the expectation of financial rewards that attracted the best men into this kind of work. They were drawn more by a true sense of vocation, and at the same time they knew that they were assured of a position in society which carried with it regard for their personal worth. The status and prestige of the general practitioner are obviously linked to a large extent with what society is prepared to pay him for his long and responsible labours. But, whatever the intentions of the Spens Committee, things have not worked out in the way that was hoped for. General practice has received a severe setback in public esteem and in the eyes of the medical profession. The general picture is such as to discourage a young man from taking up what is the most worth-while career in Medicine. Recently a final-year student asked in our columns for advice from his seniors,[1] and the replies that were published in the *Supplement* of March 3, while discouraging in parts, nevertheless did show that, whatever the complaints among general practitioners, they are made against a background of a love for the work they do and a belief that it is worth doing. Yet it is idle to deny that this spirit is being damped down by the comparisons that are now publicly made between the rewards of general practitioners and others in the medical and dental professions. It is now nearly three years since the N.H.S. was inaugurated, and there is still no agreement about what general practitioners should be receiving if the Spens recommendations are to be fulfilled. This continued postponement and delay has led to widespread dissatisfaction and sense of frustration. If this goes on much longer the N.H.S. structure, which is already beginning to creak, will begin to crack.

When the General Medical Services Committee met on Tuesday to prepare the ground for the Conference of Local Medical Committees planned to take place on March 29, they received a letter from the Ministry of Health (published elsewhere in this issue) in which it was stated that as a result of his first discussion with representatives of the G.M.S. Committee the Minister is convinced that "there is a good prima facie case for their reviewing, as a matter of urgency, both the adequacy of the total remuneration of general practitioners and its distribution." (The "their" refers to himself and the Secretary of State for Scotland.) This is at least encouraging. The new Minister of Health, Mr. Hilary Marquand, is, it is fair to assume, really sympathetic towards general practitioners, and within the limits of his powers anxious to resolve the present deadlock. Unfortunately he comes into office at a time when the profession has been put off by one pretext after another by the previous Minister, and so general practitioners have become intolerant of any further delay. But at the same time we should recognize that, new to his task and faced with this problem on the eve of the Budget, Mr. Marquand has some reason for suggesting that the review of the facts should be made not in March but in April.

The G.M.S. Committee on Tuesday of this week discussed this matter at some length. They were, of course, well aware of the anxiety of general practitioners for a solution of their problem, and some no doubt could not help reflecting upon the rapidity with which the claims of the railwaymen were met recently by Mr. Aneurin Bevan. The two matters to be settled are the expenses ratio—which surely could be settled quickly without splitting any more hairs—and the size of the central pool of money for distribution to general practitioners in terms of the recommendations of the Spens report.

The G.M.S. Committee discussed at length the question of postponing the March conference. One disadvantage of holding it on the arranged date is that certain important information will not then be available. Nevertheless the conference has already been postponed once—from December to March—because of difficulties arising from the strike in the printing industry. To postpone it once more, even though this could on some grounds be justifiable, might, it was felt, weaken the profession's position. The Committee therefore decided that no steps should be taken to postpone the conference, which will in any event have before it a letter in which, for the first time, a Minister of Health has recognized there is a prima facie case for reviewing the adequacy of the remuneration general practitioners are now receiving.

[1] Watson, P. G., *British Medical Journal Supplement*, February 17, 1951, p. 51.

CHOLERA

There has been no cholera epidemic in the United States for three-quarters of a century, or in Britain for over half a century. Most Western European countries have been equally free from this disease. Yet scarcely a week passes without a patient dying of cholera in Bengal, and the annual toll in India and Pakistan still averages over 200,000 deaths. The immunity enjoyed by western countries, however, has cost them millions of pounds annually through quarantine organizations, delays to shipping, and other trade-hampering restrictions. The true endemic areas of cholera are very limited, even in India, and the high average death rate from this disease is due to the periodic epidemics that occur when the infection spreads to the non-endemic areas. The whole world has long looked at India and anxiously waited for her to solve her own cholera problem, but the earlier measures adopted by the health authorities in India were purely palliative and consisted almost entirely in making and distributing vaccine (much of which was made, incidentally, from harmless vibrios) and in improving sanitation in the epidemic areas. It was not until the late 1920s that a more realistic attitude was adopted, and the Health Organization of the League of Nations, realizing the world-wide importance of this problem, began to stimulate, and also to assist financially, research work on cholera both in India and elsewhere. The first work was of a basic nature and consisted in the accurate identification of the cholera vibrio and the demarcation of the true endemic areas in India. The latter was not completed when the 1939–45 war stopped all such work.

After this interruption the matter was again taken up by the World Health Organization (W.H.O.), the natural successor to the Health Organization of the League of Nations. There are indications that it intends to play a more practical part in the cholera work in India than hitherto, and a combined study group of the Office International d'Hygiène Publique and W.H.O. has recently visited India and toured the endemic areas. The report[1] of the third session of this study group shows that the subjects considered were certain quarantine problems, laboratory studies, endemicity, and the W.H.O. cholera-control programme. It is apparent that there are far more outstanding problems than matters on which some decision has already been taken; the common theme in this report is that research work on the various lines should be continued. The control programme consists almost solely in steps to achieve abundant pure water supplies and suitable methods of disposing of excreta in the endemic areas. It is perfectly true that if this objective can be achieved in all the endemic areas—it is, however, a big if—cholera might be banished from the world for ever. In the meantime treatment of the individual case must remain as important as ever.

Since Koch demonstrated the cholera vibrio attempts have been made to sterilize the intestinal tract of the unfortunate cholera patient with whatever was the popular antiseptic at the time, and with each new group of antiseptics that has appeared the attempt has been hopefully renewed. The story is one of 70 years of complete failure. This is the more surprising since the vibrio is confined almost entirely to the lumen of the gut and the superficial mucosa. The most popular of the newer drugs has been the relatively insoluble sulphanilylguanidine. The results reported have been varied, but appeared on the whole to be encouraging. A typical example is the work of Chopra and his colleagues,[2] who reported a 6.9% death rate among controls, compared with 5.56% among patients treated with this drug: the difference is of little significance but is in favour of the drug. The low death rate is due in part to the effective intravenous saline treatment that was given to the patients of both groups.

A more recent result obtained with a sulphonamide drug was that of Bhatnagar and his colleagues.[3] This was a field experiment, where the patients were treated in their homes without saline transfusions. It was reported that there were 82 recoveries among 85 patients, 57 of whom were semi-comatose, with imperceptible pulses, anuria, and marked dehydration. The formula of the drug was not disclosed, but it was said to be a "molecular combination" of sulphathiazole and formaldehyde.

Perhaps not the least remarkable thing about this report is that we have heard nothing more about the drug, and there is no evidence that in a country where there is no lack of clinical material—200,000 cholera deaths annually—any attempt has been made to reproduce this remarkable result, although it is nearly three years since the report was published. However, elsewhere in this issue (p. 500) there is a report of a clinical trial with sulphanilylguanidine and two other drugs, formosulphathiazole (the name of which suggests some relation to Bhatnagar's drug) and formosulphacetamide. Lahiri obtained very different results from those of Bhatnagar. The total percentage death

[1] Joint OIHP/WHO Study Group on Cholera. Report on the Third Session. Technical Report Series, No. 18. Geneva, 1950.
[2] *Indian med. Gaz.*, 1941, **76**, 712.
[3] *British Medical Journal*, 1948, **1**, 719.
[4] Napier, L. E., *Modern Practice in Infectious Diseases*, Butterworth, 1951. London. In press.

rate among the patients on sulphanilylguanidine was 30.35%, among those on formosulphathiazole 34.37%, among those on formosulphacetamide 34.43%, and among the controls on no specific drug 18.31%. All received saline infusions as well. Thus, better results were obtained without the aid of chemotherapy. Further, daily stool examinations were carried out in a representative number—from 27 to 36 cases—in each group. In the rate of disappearance of the vibrios there was little difference between the cases treated by chemotherapy and the controls. The best result was obtained in the sulphanilylguanidine group, where the vibrio had disappeared from the stools in every case by the ninth day, whereas in the group receiving no drug vibrios had disappeared in 30 out of 36 cases in the same period. This result is admittedly in favour of the sterilizing action of the drug, though the difference is of low significance; but this was apparently not a life-saving property, as the death rate was three-fifths greater in the former series.

Cholera has been described as a self-limiting disease in which death may occur from dehydration and acid-base imbalance, or from irreversible changes produced by local ischaemia in vital organs, before antibody formation has had time to prevent or mitigate the local effect of the cholera endotoxin in increasing the permeability of the intestinal mucosa.[4] Lahiri has shown that chemotherapy does not materially accelerate the disappearance of vibrios, whereas it may be detrimental to the patient in other ways.

By the time the patient shows any definite symptoms of cholera it is probably too late for the drug to have any real beneficial action; there has been a mass multiplication of vibrios, and their destruction without coincident antitoxin production will temporarily increase the endotoxin in the intestinal tract. Whether these drugs could, however, act prophylactically is another matter. It is certainly a possibility worth exploring. A more hopeful line of treatment would be an attempt by biological or chemical means to reverse the endotoxin's action of increasing the permeability of the intestinal mucosa.

STEROIDS AND WATER METABOLISM

The direct effects of steroids on water metabolism have until recently been neglected. One reason for this has been the early emphasis on the changes in sodium and potassium distribution produced by adrenal cortical extracts, alterations in water balance being thought to be secondary to them. Admittedly, the inability of patients with Addison's disease to excrete water at a normal rate was pointed out by Rowntree and Snell[1] as early as 1931, but it was regarded as mainly the result of changes in the circulation.

Experimental evidence now suggests, however, that at least some cortical steroids may exert a direct effect on water excretion, independent of their actions on electrolyte metabolism and independent of vascular effects. In adrenal insufficiency there is a failure of the diuretic response to administered water, regardless of the salt load of the body. The action of cortical hormones on renal water excretion is not always closely correlated with alterations in electrolyte excretion, and desoxycorticosterone, the adrenal steroid most effective in causing sodium retention, has a diuretic action in many circumstances. Furthermore, adrenal cortical extracts are diuretic without changing the glomerular filtration rate, which suggests that they decrease renal tubular water absorption. Granted that steroids have this direct effect under experimental conditions, to what degree do they participate in producing clinical changes in water distribution and excretion?

The sifting and co-ordination of recent experimental evidence was attempted at a recent Ciba Conference, where it appeared that the renal effects of steroids on water and electrolyte excretion are much better understood than their extrarenal actions. This is natural, since pure kidney effects are technically easier to study than extrarenal effects, which may be complicated by secondary reactions to changed kidney function (a point emphasized by the clinical findings of Elkington[2] and Luetscher[3]), and since the visualization of the fundamental processes underlying movement of cellular ions and water has been difficult, though Conway[3] and Ussing[4] suggest that water and electrolyte movement is to some unknown extent linked to cellular metabolism.

The existence of this link helps to explain why the effects of mineralocorticoids and glucocorticoids frequently overlap, a point stressed by Verzar[3] and Zuckerman.[3] In any case caution in classifying steroids rigidly in one or the other group is certainly indicated, if only because differences in solubility, mode and duration of administration, and species differences in the response of test animals make the

1 *A Clinical Study of Addison's Disease*, 1931, Saunders, Philadelphia.
2 *J. clin. Invest.*, 1949, **28**, 99 and 378.
3 Papers read at the Ciba Conference, January 8–10, 1951.
4 *Physiol. Rev.*, 1949, **29**, 127.
5 *New Engl. J. Med.*, 1948, **239**, 353.
6 *Proc. Soc. exp. Biol., N.Y.*, 1940, **44**, 502.
7 *Science*, 1938, **88**, 150.
8 *Physiol. Rev.*, 1949, **29**, 281.
9 *Proc. Soc. exp. Biol., N.Y.*, 1949, **70**, 83.
10 *Fed. Proc.*, 1950, **9**, 12.
11 *J. Pharmacol.*, Part 2, 1950, **98**, 161.
12 Heller, H., *Experientia, Basel*, 1950, **6**, 368.
13 Chalmers, T. M., *et al.*, *J. Physiol.*, 1951, **112**, 238.
14 Sinclair-Smith, J., Sisson, J., *et al.*, *Bull. Johns Hopk. Hosp.*, 1950, **87**, 221.

close comparison of different steroids difficult. It was emphasized by Conway,[3] for example, that the effects of desoxycorticosterone and cortisone on electrolyte and water balance may be very similar, provided only that adequate doses of the latter are used. Indeed, Winter[3] could show that a condition resembling diabetes insipidus can be produced by repeated administration of either compound, apparently, however, in some degree dependent on sodium intake: animals with low plasma sodium levels are, as reported by Hayes,[3] unable to eliminate water at the usual rate even when adrenal cortical function is normal, while addition of salt to the diet raises the water exchange quite markedly. It has been suggested by Peters[5] and others that this diuretic effect is primarily due to the great thirst in sodium retention. If this were so all steroids which decrease sodium excretion should after continual administration in suitable amounts cause more water to be excreted. This has been claimed by Selye and Basset[6] to occur with progesterone, but it does not seem to apply to oestrogens and androgens. Further work is obviously needed.

Increased knowledge has also raised the question whether normal electrolyte and water excretion results from a balanced interaction of the adrenal cortex and the posterior pituitary. This theory, first formulated by Silvette and Britton,[7] has acquired additional importance through recent findings by Gaunt, Birnie, and their collaborators[8, 9] that not only are adrenalectomized rats more sensitive to the posterior antidiuretic hormone (reported also by Lockett[3] in adrenalectomized dogs), but that an antidiuretic substance found in the serum of normal rats is increased after adrenalectomy. This blood factor may indeed be of posterior pituitary origin, in view of Heller's[3] report that with Ginsburg he has found a labile antidiuretic factor in the venous outflow from the head but not in blood obtained from other sites. The increase in sensitivity and rise in the antidiuretic titre of blood after adrenalectomy may conceivably be explainable on the basis of Birnie's[10] observation that the liver of adrenalectomized rats is less potent than that of normal animals in inactivating vasopressin.

Be this as it may, the concept of a simple antagonism between adrenal and posterior pituitary must at present be approached with considerable caution. It is, in particular, unlikely to apply to the renal excretion of sodium and chloride (as recently suggested by Pitts and Sartorius[11]) and certainly not to that of potassium. The excretion of potassium by the kidney is increased by both posterior pituitary[12] and adrenal cortical extracts, and it has now been shown that the antidiuretic action of vasopressin may occur without any rise in sodium and chloride elimination.[12] It certainly does so in human beings.[13, 14] However, it would be reasonable to expect a regulatory response of the neurohypophysis to any major distortion of water metabolism resulting from adrenal insufficiency. The finding of Heller[3] and Birnie and Heller,[3] that the kidneys of infant rats begin to respond to posterior pituitary and to adrenal cortical extract at much the same period after birth, is perhaps a further hint at an adrenal–posterior-pituitary relationship.

ADJUSTMENT TO BLINDNESS

Doctors have few more distasteful tasks than having to inform a patient that nothing can restore his sight or save what little may be left. If the patient has considered what blindness would mean to him personally—and in many cases that thought is inhibited—he is likely to assume that the rest of his life will be a dull and dreary round of deprivations and dependency. Fortunately the information contained in the recently published report[1] of the working party on the employment of blind persons shows convincingly that such an assumption is unjustified. Its main conclusion is that loss of sight does not in itself debar men and women of working age from employment in numerous industrial, commercial, and professional occupations. Without subsidy or compassionate consideration they can hold their own, resuming their place as producers, doing a full week's work for a full week's wage, or practising certain professions. This comparatively new view of blind welfare is based on the work of St. Dunstan's for Servicemen blinded in early manhood and on years of research and experiment by the National Institute for the Blind.

The report of the working party emphasizes that people who fall within the official definition of blindness are not for that reason sick persons. "The blind" are in fact an almost haphazard sample of the general population, with its infinite variety of individual temperaments, aptitudes, and interests: they are differentiated simply by inability to use a sense on which sighted persons chiefly rely. It is too often assumed that only individuals of more than ordinary character and capacity can successfully overcome the grave handicap that blindness must always be. In effect the working party's slogan might have been, "Normal Life for the Normal Blind." This fresh attitude is not the result of a new discovery of what the blind can learn to do by touch and "muscular memory" (though research has thrown fresh light on that) so much as a new appreciation of the scope of rehabilitation. To learn to read and write in braille is only one move in what has been aptly called "the recovery of confidence and competence." The newly blinded person has first to be convinced that

[1] Report of the Working Party on the Employment of Blind Persons, 1951. H.M.S.O., London.

he can still enjoy life and play a useful part in it. Then he has to learn how to use hearing and touch, and even smell, more intensively and more accurately than when his eyes gave him quick and easy interpretations and guidance.

Rehabilitation, in any real sense of the term, may be impossible unless undertaken away from home. The working party reserves judgment on an experiment of the London County Council in rehabilitation by classes, but there is no doubt about the value of home-visiting by qualified home teachers, who can catch the newly blinded man or woman before he or she falls into bewilderment or despair. The home teacher may also be able to warn the family that the consequences of trying to do everything for a blind person may be disastrous. But, whether the main object is social or industrial adjustment, rehabilitation at a residential centre is advisable for "substantial numbers" of people of working age. The National Institute's "Home of Recovery" at Torquay has recently more than doubled its accommodation, but it has a long waiting-list and there is urgent need for the establishment of another centre in the north of England. The purpose at Torquay is not to teach a trade but to rebuild self-confidence on personal achievement and to judge capacity for employment. Technical training for an occupation is carried out by the Ministry of Labour at the Government Training Centre in Letchworth, or on the job under the supervision of an N.I.B. employment officer. In carrying out the new policy for the blind the Ministry of Labour makes use of, and supports financially, voluntary bodies, which are left free to do the work they best understand.

The conspectus of occupations open, but in some cases not yet wide open, to the blind indicates pretty clearly what a newly blinded person can hope to do. Basket-making need not remain the staple industry. Blindness has proved no impediment to clergy and ministers, solicitors, and musicians. School-teaching is only for blind persons with exceptional gifts. At the universities professorships and other important posts are held by blind men. Wider opportunities should be given in public administration to blind people of proved capacity. Blind shorthand-writers and telephonists, already valued in many offices, could be employed with advantage in more. In industry, particularly light engineering, there are hundreds of processes in which blind workers give at least average output. As to physiotherapy, the working party was "impressed by the virtual unanimity with which witnesses who have had experience of employing blind physiotherapists have testified to their high qualities and professional competence." With at least 15,000 physiotherapists in practice, there need be no anxiety about the employment prospects of the limited number—never likely to exceed 400—of blind persons who reach the high standard required by those who are responsible for their selection and training. Indeed, emphasis is placed throughout the report on the skill required in education, rehabilitation, training, vocational guidance, and placement. The conquest of blindness is a challenge to character which, as a rule, is unflinchingly met. But the individual's struggle must be supported by a service which is efficient, profoundly understanding, yet unsentimental and practical.

CHOLINE AND ATHEROSCLEROSIS

Of the various factors possibly concerned in the causation of atherosclerosis the one which in recent years has received the most attention is the disturbance in lipid metabolism. This is shown by the presence in the lesions of cholesterol and its esters, phospholipids, and fatty acids, and in the fact that in those conditions in which hypercholesterolaemia may occur—such as diabetes, nephrosis, and severe hypothyroidism—atherosclerosis is commonly more severe and tends to develop at an earlier age. Further, in 1913 Anitschkow[1] showed that atheromatous lesions developed in rabbits after feeding with cholesterol, and Scarff,[2] confirming this, found that when rabbits, after a period of cholesterol feeding, were put for six months on a normal (low cholesterol) diet the atheroma did not regress but came to resemble human atheroma still more clearly. Recently Gofman and his associates[3] have detected a serum lipo-protein fraction absent in normal rabbits but present in considerable quantities in cholesterol-fed rabbits. In man he found small quantities in young adults, large amounts in older individuals, and most in diabetics and those that had had a myocardial infarction. The amount of this material in the serum did not invariably run parallel to the serum cholesterol, and it is possible that an explanation has here been found of the fact that a normal serum cholesterol is frequently found with atherosclerosis.

If there is good reason to believe that a disorder in lipid metabolism plays an important part in the causation of atheroma there is little experimental evidence to justify the use of a low-cholesterol diet in the treatment of this condition, and clinical experience has provided no more. Moreover, Kay and Michelson[4] have shown that blood cholesterol values are not significantly affected by wide variations in cholesterol intake and that the mere avoidance of cholesterol-rich food is unlikely to lead to a fall in serum cholesterol. They found, however, that a rice–fruit diet, which is cholesterol-free and contains very little fat, lowered the average serum cholesterol in a group of cases from 232 to 152 mg. per 100 ml. in three weeks. It seems then that if the course of this disease is to be influenced dietetically a much stricter diet is necessary than is usually contemplated.

A more promising approach has opened up from Best's observation that choline deficiency leads to the deposition of fat in the liver, and choline administration to its removal. Morrison and Rossi,[5] confirming

[1] *Beitr. path. Anat.*, 1913, **56**, 379.
[2] *J. Path. Bact.*, 1927, **30**, 647.
[3] *Science*, 1950, **111**, 166.
[4] Ibid., 1950, **112**, 79.
[5] *Proc. Soc. exp. Biol., N.Y.*, 1948, **69**, 283.
[6] Ibid., 1938, **39**, 411.
[7] Ibid., 1950, **73**, 37.
[8] *Amer. Heart J.*, 1950, **39**, 729.

Steiner's[6] work, have shown that experimental atheroma in rabbits could be greatly improved by choline feeding, and in recent papers Morrison and Gonzales[7 8] have recorded the results of choline therapy on the death rate among patients during a period of 1–3 years after their first coronary thrombosis. Two hundred and thirty patients consecutively admitted to Los Angeles General Hospital were used for this investigation, the series having been divided into two groups by placing alternate patients in each. In sex, age, symptoms, and blood pressure the groups proved similar. The treatment group was given choline bicarbonate by mouth in doses varying from 6 to 32 g. daily, while the control group received symptomatic treatment. For part of the period both groups had dicoumarol treatment. During the three years of the investigation 30% of the control group died and 12% of the choline-treated group. This difference is statistically highly significant. Gastro-enteritis limited the maximum dose taken by many of the patients, but those able to tolerate a large dose showed most marked improvement. No other serious side-effects occurred.

Further carefully controlled experimental work is needed before the place of choline and other lipotropic agents in the treatment of atherosclerosis can be assessed. Clearly they are unlikely to have much effect on any but relatively recent deposits, but a most promising line of investigation has been opened by these findings.

SILICOSIS IN FOUNDRY WORKERS

In the last 20 years great interest has been shown in the industrial lung diseases of foundry workers, and more than 25 clinical or radiographic surveys have been undertaken in a dozen countries. In Britain, steel fettlers and dressers have been able to get compensation for silicosis, and also shot and sand blasters, but foundry workers generally have not been considered subject to any appreciable risk. The occurrence of three deaths from silicosis among iron moulders at one particular factory drew attention to the possibility that the risk might be greater than had been suspected, and a thorough investigation of the whole subject was evidently desirable.

Iron dust by itself may be deposited in the lungs and give rise to radiographic changes; but there is no secondary fibrosis, and siderosis does not appear to cause any disability. Most foundry workers are, however, also exposed to silica dust and consequently to the risk of silicosis. The two main divisions of the foundry are the moulding and fettling shops: in the former dust is raised by the process of making the mould out of sand, and in the latter by the process of cleaning the fresh casting (i.e., by fettling). Foundry men not directly concerned in either process may, however, have to work in the same general dust-laden atmosphere. The number of cases of silicosis among steel fettlers coming to the notice of the Silicosis Board is steadily increasing each year. According to McLaughlin,[1] whose study of the subject was published last year, this can be attributed to the increasing use of pneumatic drills in place of hand tools for cleaning the casting. Fettlers in steel foundries would appear to be more subject to silicosis than fettlers in iron foundries, because the sands used for making the moulds contain higher proportions of free silica and because the higher temperatures at which the metal is cast cause the sand to adhere more firmly to the casting.

McLaughlin has also reported the results of a survey undertaken by a team of experts to determine the extent to which all grades of iron and steel foundry workers develop pulmonary abnormalities. Men from 17 different foundries, 2,767 in all, were interviewed and examined clinically and radiographically; some were also submitted to exercise tolerance and vital capacity tests. Abnormal radiographic findings were classified as early reticulation, reticulation, and nodulation with or without massive shadows. It is doubtful whether much significance can be attached to the cases described as early reticulation, since it was also found to an appreciable extent among workers who were not thought to have breathed silica dust (for instance, pattern makers). Reticulation or more marked changes were found in 34% of fettling-shop workers in steel foundries, in 13% of men in mixed steel and iron foundries, and in 12% of men in iron foundries. Similar pulmonary changes were found in 13%, 8%, and 7% respectively of moulding-shop workers in these three types of foundry. Silicosis would therefore appear to be a common finding in steel fettlers and to be present to some extent among iron fettlers and among workers in both iron- and steel-moulding shops.

More detailed conclusions cannot be drawn, since the proportions of workers examined in the different trades and in the different foundries were so variable—being, in fact, anything between 21% and 100%. In fact, the main conclusions are unlikely to have been invalidated, but quantitative comparisons between small groups must be highly unreliable. One wonders to what extent the inconvenient physical examinations may not have contributed to the men's reluctance to be interviewed; concentration on interview and radiographic examination might have resulted in the survey being more complete and consequently more useful. Nevertheless, it is clear that silicosis does occur in iron- and steel-foundry workers and that a problem of preventive medicine exists. That this should be the case can hardly be a surprise to anyone who has ever visited a foundry. Much could undoubtedly be done by improving dust suppression—many foundries appear to have remained in the state in which they were first designed—but it may also be possible to substitute an innocuous substance for the silica used in preparing the moulds. Olivine, which has been introduced with success in Scandinavia, is one such substance.[2]

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1 *Industrial Lung Diseases of Iron and Steel Foundry Workers*, 1950, H.M.S.O., London.

2 King, E. J., Rogers, N., Gilchrist, M., Goldschmidt, V. M., and Nagelschmidt, G., *J. Path. Bact.*, 1945, **57**, 488.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

EMPHYSEMA

BY

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Pulmonary emphysema is a term that has come to be applied in a rather loose way to a number of conditions which, aetiologically speaking, are quite dissimilar. We speak of large-lunged and small-lunged emphysema, the former conjuring up visions of breathless bandsmen (who may have been drummers) and the latter of leaner, more scholarly individuals. Then there are interstitial emphysema, compensatory emphysema, and that peculiarly localized variety spoken of as bullous or cystic emphysema. Despite their apparent dissimilarity, there are features which unify all these varieties. These are loss of elasticity and the destruction by rupture of interalveolar septa.

Pulmonary Distension

Among the essential properties of lung tissue an important place must be given to elasticity and the power to inflate and deflate. It is a prerequisite of our existence that this inflation and deflation should take place. The capacity of the lungs to contain air varies enormously: a fit man has little difficulty in blowing three litres at a "vital capacity" determination, and all this air must have been accommodated in full inspiration by the stretching of pulmonary tissue and bronchi, and alteration of their mutual relationships. This expansion and recoil repeats itself about a thousand times in each hour in health. With the passage of years, even in the absence of disease, changes take place. In particular, the recoil diminishes and elasticity gives place to rigidity, fixity, and shrinkage—to small-lunged emphysema of the elderly.

A similar loss of elasticity is produced after some years of pulmonary distension: shrinkage of part of the lung owing to collapse or disease will necessitate compensatory changes, and if these cannot be wholly met by shift of the heart and mediastinum there will be overdistension of the parts of the lung which are still aerating. Compensatory or hypertrophic emphysema may for a time be a true description of this process, but later the continued overstretching will produce distension beyond the limit of reversal.

Rupture of the interalveolar septa is a feature, in greater or lesser degree, of all varieties of emphysema. It is seen in its grossest form in the bullous or cystic variety. Here, the very property of inflation is turned to a disadvantage. Some minor alteration in the relationship between bronchial tube and pulmonary tissue permits distension of an area of lung without the possibility of its deflation. Septal rupture proceeds apace and a localized pulmonary balloon within the lung results. This same process, essentially, operates in inflammatory disease; in certain varieties of bronchopneumonic affection and in tuberculosis with lesions of important extent in bronchial tubes it makes possible the development, from a small area of destructive pulmonary breakdown, of a tension (or, as it might equally well be termed, a distension) cavity. It is probable that up to a certain limit of distension, and perhaps depending to some extent on the duration of the distension, the process may be a reversible one. Once this limit has been passed the process is irreversible.

Generalized bronchial inflammation, particularly if associated with bronchial spasm, is likely to lead to emphysema. In the production of cystic or bullous emphysema the state of affairs is postulated where the obstruction to the outlet of air is complete or nearly so. In bronchitis with spasm, well exemplified in chronic recurrent asthma, the obstruction is not complete, but over weeks and months it exerts a telling effect. Intimately connected with the whole subject is the fact that while inspiration is a powerful movement, involving active work for various groups of muscles, expiration is in the main passive, at least so far as costal respiration is concerned. This means that it is easier to inflate (or distend) the lungs than to deflate them. In fact, it is only by cultivation of diaphragm breathing that really forcible expiration is possible. The bearing which this functional distinction between inspiratory and expiratory movement has on pulmonary distension will be obvious.

Pulmonary Reserve: Effect on Function

Increasing experience of patients who have had a pneumonectomy or lobectomy, or of individuals in whom some disease process has reduced the available pulmonary tissue, is bringing a fuller realization of the immense reserves of respiratory function of which human beings are possessed. Equally striking is the dire plight of patients who have had a pneumonectomy after a faulty assessment of their reserves. Considerable damage must have accrued over the years in an individual before symptoms are produced by emphysema. On the whole, the younger the subject of lung ablation, whether surgical or the result of disease, the better is his adjustment. Emphysema produces some degree of anoxia. The total surface area over which air and haemoglobin can make contact is reduced. The distension obliterates altogether some capillaries and reduces the lumen of others. The air tends to be drawn into the relatively distended peripheral parts of the lung, and the impaired expiratory force makes for the stagnation of air there and hinders its replacement with fresh atmospheric air containing the normal complement of oxygen. All these factors make emphysema a serious disability.

Further aggravation may come through the operation of the Hering-Breuer reflex. Normally the impulse to terminate the process of inspiration arises in pulmonary stretch receptors. When a certain degree of lung distension has been reached these receptors are stimulated, inspiration ceases, and expiration begins. If there is gross localized emphysema, as for instance in bullous or

cystic emphysema, stimulation of the receptors may occur in the distended portion of lung, while the remainder is still capable of some expansion which, from the functional point of view, would be profitable.

Diagnosis

Emphysema is often diagnosed, and in many cases probably correctly so, but it is by no means easy to lay down reliable criteria for its recognition. It can occur as an acute process, though it is more frequently encountered as a chronic and static phenomenon. Sometimes there is a familial incidence. Patients are often in early middle life and their complaint is breathlessness. They are particularly troubled on exertion, when they may show a tinge of cyanosis.

The conformation of the thorax and the posture of the ribs often indicate some overdistension of the lungs. Measurement shows poor thoracic expansion, often less than 2 in. (5 cm.) being evident between full expiration and full inspiration. There may be hyperresonance and obliteration of liver and heart dullness, though these findings are frequently equivocal. With the stethoscope one is often struck by the poor air-entry and the very quiet respiratory murmur. Prolongation of expiration and added sounds, particularly rhonchi, are features of associated bronchitis and bronchial spasm rather than of emphysema itself. The radiographs are often striking. The ribs lie in an exaggerated inspiratory position, the outline of the diaphragm is ragged with a scalloped outline, and the heart shadow is narrow. One gets the impression of overdistended lung from the unduly black appearance of the parenchyma. If there are grossly localized areas of emphysema, they are often readily apparent, and sometimes the walls of cystic or bullous spaces can be traced as hair-like lines.

Chronic bronchitis may be the sequel of an acute attack or it may develop insidiously in association with emphysema. The two conditions are intimately connected and emphysema is undoubtedly aggravated by chronic bronchitis, more especially by exacerbations of acute bronchitis. The four months from November to February are the critical ones for bronchitic patients. They mostly lose time at work each year after the age of 50. As the years go by acute exacerbation tends to occur earlier in the winter, and it may be repeated once or twice before the spring.

Management

With degenerative changes at work and so much structural alteration in being it may well be thought that little enough can be done to help emphysematous people. The treatment of emphysema falls under three heads: (1) the prevention and cure of attacks of bronchitis with spasm and of asthma; (2) the institution of measures to produce the maximum use of the available pulmonary tissue and particularly to develop expiration; and (3) the consideration of any procedures which may be indicated to meet special varieties of emphysema.

It should be an axiom that bronchial spasm should be relieved as quickly and effectively as possible whenever it occurs. Once that pattern of functional behaviour which results in spasm of the bronchial wall has been set, the pathway to its production is facilitated and the spastic response to various stimuli occurs all too readily. Whatever remedy has been found to be most efficacious in an individual case, whether it be an antispasmodic drug, a member of the antihistamine series, or one of the varieties of adrenaline or ephedrine, it must be used early and in adequate doses. In the bronchitis of middle-aged and elderly people it often pays to saturate the patient with an antispasmodic, and that good old-fashioned remedy "iodide and stramonium" has few equals.

Potassium iodide	3 gr.	(0.2 g.)
Tincture of stramonium	15 min.	(0.9 ml.)
Liquid extract of liquorice	30 min.	(1.8 ml.)
Spirits of chloroform	5 min.	(0.3 ml.)
Water	to 1 fl. oz.	(28.4 ml.)

It should be taken regularly, not intermittently, until a full week has elapsed after the relief of symptoms. Penicillin and the sulphonamides have a distinct place in these cases, though their value is often discovered only casually when they are being given for some other condition, as, for instance, a urinary infection. Antibiotics are best given by injection; sulphonamides should be used in orthodox doses, to a total of 35 g. in a week. Inhalation therapy can sometimes be most valuable, but, whatever proprietary preparation is used, the instructions supplied with the form of apparatus concerned should be followed in exact detail.

To experience more than one exacerbation of acute bronchitis during a winter is very discouraging and the condition is often prolonged well into the spring. For the few who can manage it, three weeks spent at one of the French spas may help them to a better level of health. Prevention of bronchitis in those who are subject to it may involve a change of habits or even of work. Patients with this sort of chest trouble are often advised that they should have an outdoor job. Generally speaking, indoor work is to be preferred in Britain. As Sir Clifford Allbutt put it many years ago, "fresh-air treatment does not mean treatment by hurricane." Far too often the climatic conditions encountered in this country between November and March are such as to aggravate very seriously the bronchitic tendency. Restrictions must be accepted, and going out on cold, raw winter nights, especially when fog may be encountered, should be forbidden. Any abrupt change from warm to cold is a potential aggravating factor. The acceptance of this way of life will certainly have a preventive value, and it is essential if the bronchitis and emphysema are merely additional burdens in a respiratory system already impaired by scarred and fibrotic tubercle or other established disease.

Somehow or other an attempt must be made to improve the resilience of the thorax. The barrack-square ramrod posture, a lunge forward with the arms flung wide to greet the wintry dawn at an open window, is an approach as wrong as it can well be. Rather should the emphasis be on relaxation, with the patient lying down comfortably on a couch endeavouring to dispel all tension. Then when he is calm he makes a deliberate effort to move and control the diaphragm. The facts about diaphragm movement, and what it can achieve, and its particular value in expiration are explained to him. He must make a conscious effort to cultivate diaphragm breathing and lower-rib expansion. He must watch himself in a looking-glass part of the time to break the habit of upper respiratory breathing with tensing of the sternomastoids and trapezii and elevation of the whole shoulder girdle. He must practise his diaphragm diligently until the movement is second nature to him.

Just occasionally some special measures may be applicable. The induction of a pneumoperitoneum can

certainly give a ragged diaphragm a smooth contour, but on the whole the long-term results have been disappointing. Some unfortunate results also have attended well-intentioned efforts to remove emphysematous bullae or cysts. There is some evidence, however, that, paradoxically enough, a phrenic interruption may be beneficial in cases of gross localized emphysema at a base where the reflex control of respiration is dominated by the distension in this situation. When some relaxation is produced inspiration and expiration of the less distended parts of the lungs assume more normal proportions and rhythm.

DR. HELEN KELLER IN ENGLAND

On the eve of her departure from this country to South Africa Dr. Helen Keller was the guest of honour at a dinner-party given by Sir Ian and Lady Fraser at the House of Commons on Wednesday, February 28. Dr. Keller was accompanied by her lifelong friend and guide, Miss Polly Thompson, through whom she has contact with the world around her, and by Mr. Alfred Allen, the assistant director of the American Foundation for the Blind. A distinguished and representative company was gathered to pay tribute to

Sport and General Press Agency, Ltd., London]

Dr. Helen Keller in conversation with Sir Ian Fraser.

Dr. Keller's courage and example. At the age of 2, following an attack of scarlet fever, she was deprived of sight, hearing, and sense of smell; yet in spite of these great handicaps she has not only learnt to talk and to communicate her ideas but has achieved high academic distinction in letters, languages, and mathematics, as well as world-wide fame for her work among the deaf-blind. There were at the dinner representatives from St. Dunstan's and the National Institute for the Blind, Members of Parliament from both sides of the House, M. Georges Raverat, European director of the American Foundation for Overseas Blind, and among the other guests Maestro J. Rodrigo, a noted blind Spanish composer.

Sir Ian Fraser, welcoming Dr. Keller and Miss Thompson, said that as one born in South Africa he was glad that they were to visit that country to see the organizations there for the care of the blind and the deaf. He was sure that Dr. Keller would bring help and encouragement to all handicapped people in the Union, whether European, Indian, or African. Sir Ian Fraser's speech was interpreted to Dr. Keller by the movements of Miss Thompson's right hand in her own, and it was clear from the lively expression of pleasure on Dr. Keller's face how much she appreciated what was said. It was easy to see how completely she was able to participate in all that went on, and this became even more evident when she rose to reply to Sir Ian's toast. Her words required Miss Thompson's sympathetic interpretation, but it was remarkable how distinct were some of them, especially those which were charged with feeling. In a most gracious speech she thanked her hosts and all those who had come to welcome her.

Miss Florence Horsbrugh, M.P., then proposed the health of Maestro Rodrigo, who lost his eyesight after diphtheria when he was 3 years old. She told the company how, in spite of this handicap, he had become a professor of music at Madrid University; how he had recently composed a concerto for guitar and orchestra in braille, which was later transcribed by a copyist.

REMUNERATION OF GENERAL PRACTITIONERS

LETTER FROM MINISTRY

The B.M.A. has received the following letter from the Ministry of Health:

"I am directed by the Minister of Health to refer to the meeting between representatives of the General Medical Services Committee and the Secretary of State for Scotland and himself on February 28, and to say that the Minister himself is already convinced, as a result of his first discussion with the representatives—and the Secretary of State for Scotland agrees—that there is a good prima facie case for their reviewing, as a matter of urgency, both the adequacy of the total remuneration of general practitioners and its distribution. They will look without delay at the best way of speeding up that review.

"A further meeting will be arranged before the end of April."

A new amino-acid, hitherto unknown in Nature, has just been prepared from human urine by C. E. Dent and his collaborators (*Nature*, February 24, p. 307). It is a normal constituent of urine, but in 4.8% of 459 healthy people who were tested it was present in an unusually large amount. Since in these people the blood level of the new amino-acid was not raised, the authors argue that the unusual urinary excretion must be due to a low renal threshold (defective reabsorption by the tubule from the glomerular filtrate), as is the explanation of the amino-aciduria of cystinuria and Fanconi syndrome. The new amino-acid is α-methyl-β-alanine (or β-amino isobutyric acid); β-alanine has already been frequently met in biochemical work, since it is one of the two components of the B-complex vitamin called pantothenic acid, and also occurs linked to another amino-acid, histidine, in the substances carnosine and anserine, which occur in fair quantity in muscle and which are at present of unknown function or significance. Whether α-methyl-β-alanine has any metabolic connexion with them remains to be seen. The new amino-acid was discovered through paper partition chromatography of urine, using phenol and collidine-lutidine as solvents. When the paper was sprayed with ninhydrin to detect the dispersed spots of different amino-acids an unknown "T-spot" was noted: the cause has proved to be α-methyl-β-alanine.

Reports of Societies

THE ACUTE ABDOMEN IN GENERAL PRACTICE

On February 28 at their fourth meeting members of the recently formed Section of General Practice of the Royal Society of Medicine chose to discuss a condition which, as one speaker said, "stalks like a spectre through the G.P.'s life." And so a large and interested audience listened for two hours to the backbone of the profession, presided over by Dr. George Abercrombie, grappling with the problem of "The Acute Abdomen." To this meeting the Section of Surgery had been invited, and your reporter was able to observe that the ratio of semi-stiff collars and cigarettes to Clapham Junctions and cigars was roughly unity: so that both sides were fairly evenly represented.

Dr. DAVID MENDELSSOHN HUGHES introduced himself as a country practitioner living nine miles from the nearest surgeon and 35 from the nearest consultant. His carefully prepared and excellently delivered paper was a joy to listen to. Here were the personal anecdotes which would make the basis of a novel or a film, the difficulties of diagnosis in cottages and transport through floods which should make the consultant, with all his aids-to-everything laid on, feel a trifle ashamed. It was to the subject of appendicitis that Dr. Hughes devoted most of his time, and this was not surprising in view of the comparative excess of this condition over all other emergencies. It came as somewhat of a surprise to be told that in a partnership of three, with 7,200 patients and over a period of five years, only 128 acute abdominal emergencies had been seen, but of these no fewer than 87 had been "appendixes." The speaker himself in ten years had seen only three perforated ulcers and three strangulated hernias: on the other hand he had had 45 cases of appendicitis out of 72 acute abdomens.

The Smell of Appendicitis

So much for figures. In his clinical description Dr. Hughes expressed himself in phraseology which could not be improved upon in any textbook: those listening would better have been students than doctors to appreciate it fully. He called attention particularly to the remission of symptoms which frequently occurs some 12 hours after the onset of the disease, and therefore the necessity of making up one's mind at the first visit, Indeed, there should be no second visit: once the diagnosis has been made neither flood nor fog should prevent the patient being taken to hospital. It was necessary that the general practitioner and the surgeon should know each other well and trust each other's judgment if this remission of symptoms was not to prevent a patient being operated upon at the earliest opportunity. Of the many classical physical signs, he thought that the characteristic smell of the breath should be more widely recognized. So specific was this that he supposed it should be possible to train a pointer (or a setter) to point (or set) at a patient with appendicitis. In parentheses, he recalled how a dog of his used to accompany him on all his midwifery cases and await the birth of the baby. "But of course," he explained, "she was a retriever." Other speakers later on confirmed the impression of a peculiar and characteristic fetor associated with appendicitis. One doctor would have none of this, but as Dr. Hughes said in effect when summing up—either you can smell it or you can't, and that's all there is to it.

Mr. DICKSON WRIGHT, that well-known raconteur of a more fundamental Section of the Royal Society of Medicine, delighted his audience with his wit and logic. To an evening which was anyway full of aphorisms, and those in several languages, he added two memorable ones of his own: "A violent abdominal pain is surgical," and, "The medical case sits up, the surgical case lies down." He regretted that it was not possible to dogmatize to a greater extent over the acute abdomen owing to the inevitable and not infrequent atypical case. Of appendicitis, he said that the chief diagnostic difficulties arose in the very young, the very fat, and the very old. Much of his paper was devoted to the acute emergencies which did not require operations: renal colic (with its "frightful" pain), mittelschmerz, pancreatitis, acute diverticulitis, salpingitis, and—not to be forgotten—uraemia. Salpingitis, particularly, needed discrimination in diagnosis, and experience showed that help might be obtained in unlikely ways. "For instance, at St. Mary's," he added dryly, "we tend to regard a Maida Vale address with suspicion." The value of a plain *x*-ray picture of the abdomen was perhaps not fully appreciated in arriving at a diagnosis.

Help from Embryology

Mr. P. G. C. MARTIN invited his hearers to cast their minds back to their early student days and to the study of embryology. The gut was formed in three parts, and to these the nerves and vessels ran in the coeliac, superior mesenteric, and inferior mesenteric axes respectively. Abdominal visceral pain was therefore felt in a generalized fashion in different regions of the belly according as the fore-, mid-, or hind-gut was affected. Localized pain developed later and was due to irritation of the parietal peritoneum. Bearing in mind these simple facts would give much help in differential diagnosis.

A general practitioner said that he had noticed that patients with acute abdomens did not smile at the doctor when he arrived to see them. The corollary of this, said Mr. Dickson Wright, was that the doctor should avoid making silly jokes to these patients. But such simplicity was foreign to another speaker, who spoke of what he called the "pseudo" acute abdomen and the value which he attached to simple [*sic*] investigations such as the blood sedimentation rate and the potassium/calcium ratio in the blood. Mr. GEOFFREY PARKER asked what advice he should give the general practitioner about the treatment of haematemesis. Nobody told him, however. Mr. G. BLACKBURN pointed to errors in diagnosis due to placing too much reliance on the "silence" of an abdomen or upon skiagrams which showed fluid levels. He stressed that the diagnostic error in appendicitis increased considerably with the age of the patient.

Curiously enough, it was left to almost the very last speaker to mention children, their extreme capacity for having abdominal pain, and the importance of mesenteric lymphadenitis as a cause of this. With time running short and the president fingering the red light the matter was hardly discussed at all, a strange omission when one considers the number of youngsters with whom a general practitioner must come into contact.

MODERN VIEWS ON HAEMOPHILIA

At a meeting of the Section of Pathology of the Manchester Medical Society on February 14 Dr. R. G. MACFARLANE read a paper on haemophilia. He said that the nature of the clotting defect in haemophilia had been studied for many years. Available evidence suggested that the slow clotting of haemophilic blood was due to a deficiency of the intrinsic thromboplastic activity of the blood itself. This intrinsic activity normally depended upon a plasma factor, platelets, and contact with a foreign surface. It appeared that the plasma factor was deficient in haemophilia, and the corrective effect of normal plasma *in vivo* or *in vitro* was due to its content of this (antihaemophilic) factor in excess. Work at Oxford suggested that the antihaemophilic factor was not itself a precursor of thromboplastin but a co-factor which potentiated its action.

New Varieties

Haemophilia occurred in various forms. In hereditary haemophilia it was a sex-linked recessive character almost certainly due to a defective gene located on the X-chromosome. All the daughters of a haemophilic male would be carriers of the defect, and the children of such

carriers had an equal chance of being normal or affected. In the rare marriages between a haemophilic male and a female carrier homozygous females might be produced who would exhibit active haemophilia. About 30% of haemophilic subjects had no family history and were probably due to mutation. An exactly similar sex-linked condition occurred in dogs, and breeding experiments had borne out genetic theory. Lastly a similar clotting defect might occur as an acquired condition in otherwise healthy adults, most of the cases described being women soon after parturition. The probable presence of an antibody active against the antihaemophilic factor had been demonstrated in at least one of these cases.

Diagnosis and Treatment

The diagnosis of haemophilia depended as much on clinical and genetic data as on laboratory findings. Simple coagulation time determinations usually showed a significant prolongation but might be normal. The prothrombin consumption test was a more sensitive index of the haemophilic defect than the simple clotting time, and nearly all cases of so-called mild haemophilia gave significantly abnormal results. A more specific test was the titration of the antihaemophilic factor present in the patient's plasma, estimated by its ability to correct the clotting defect in the blood of a known haemophiliac. An important problem was the recognition of female carriers. Despite claims by other workers it had been found that the majority of carriers showed no defect which could be demonstrated by existing methods. A small proportion of them had minor degrees of abnormality, and it was possible that future work might establish a method of general recognition.

The treatment of haemophilia was still largely ineffective. Death from loss of blood could usually be prevented by local measures or transfusion, but the occurrence of internal bleeding could not be prevented. Only the transfusion of fresh blood or plasma, or preparations containing the antihaemophilic factor, would effectively reduce the clotting time of haemophilic blood *in vivo*. Even then certain patients failed to react, probably because of immunization by the antihaemophilic factor, which seemed most likely to occur when plasma fractions were used rather than whole blood or plasma. Probably the most effective advance would be the ability to recognize the carrier female before she produced haemophilic children. Then, with proper education and persuasion, the number of haemophilic subjects could probably be reduced to a fifth of their present total in one or two generations.

A little while ago *The Times* had a short article on Dr. Richard Russell (1687–1759), who believed strongly in the curative value of sea-bathing and is often regarded therefore as the founder of Brighton, which, under the name of Brighthelmstone, was a small fishing town of less than 2,000 inhabitants in 1750, the year in which Russell published his book on the use of sea water in diseases of the glands. He believed that the sea water should be drunk like spa water, and there was for a time an industry in being to bottle Brighton water and sell it in London. He said that fishermen never suffered from scrofulous diseases, that their wives had good complexions and good teeth, and that in his experience pale, delicate, glandular children returned from the seaside in a cured and healthy state. His book in 1750 was written in Latin and quickly went into six editions: pirated editions soon appeared also in English, and the work had an extremely wide vogue throughout Europe. Brighton became fashionable, and its population trebled in 50 years. Russell was the son of a surgeon-apothecary at Lewes, and while apprenticed to his father eloped with the daughter of one of their wealthiest patients, William Kempe, who subsequently became reconciled to him and assisted him to graduate in medicine at Leyden. He thereafter practised in Lewes, but, when his book had made him famous, moved to Brighton, and there spent the last six years of his life.

Correspondence

Operating Theatre Technicians

SIR,—As president of the Association of Operating Theatre Technicians I would like to say I am glad the *British Medical Journal* has given some publicity to this excellent association. Those of us who have had considerable experience of the good work of operating theatre technicians are convinced that their status should be established. Both surgeons and anaesthetists have much to thank these men for. With the many changes of nursing staff in the modern operating theatre the help they give us is great, and it is comforting to us to know that there are technicians who are reliable, skilled, and always available when they are needed, and that they keep instruments and apparatus in first-class working order.

To my mind the nursing profession should welcome this association as a help to its already strained resources. These technicians should not be classed as theatre porters but should be given higher status, which I sincerely hope will be forthcoming.—I am, etc.,

London, W.C.2. CECIL WAKELEY.

SIR,—I would like to express my complete agreement with the views of Drs. J. Alfred Lee and T. C. Thorne (February 24, p. 417). Those of us who have had the good fortune to give anaesthetics in a hospital where a technician is employed will need no reminder of the excellent service rendered by these men in the anaesthetic room. The chief advantages to the anaesthetist in having a technician are in the time saved preparing the apparatus, syringes, etc., before starting a list and in the general servicing of the armamentarium of the modern anaesthetic-room with its numerous perishable rubber accessories—a matter which is often perforce neglected by the overworked theatre-sister and her staff. In these circumstances it is particularly unfortunate that the regional boards should see fit to refuse to recognize the Association of Theatre Technicians and, as your correspondents state, to class these men as "orderlies."

It is to be hoped that early recognition of their services will be forthcoming and also that the number of training centres for technicians will be increased. That the answer to both these problems is only a matter of time is, I feel, quite certain; the only question is—how long?—I am, etc.,

London, N.6. M. H. W. HOLLOWAY.

Spens Awards for Professors

SIR,—As a student of the National Health Service Act, 1946, I am moved by the last paragraph of your leading article (February 24, p. 400) to ask whether I am correct in my construction of the matters under review. I take it that the following assumptions are common ground:

First, that the merit awards were instituted as part of the "emoluments of the National Health Service."

Secondly (to quote page 38 of the *National Health Service*, by Hill and Woodcock, citing the specialist Spens report), "a specialist engaged part-time in the Service, on whom a distinction award is conferred, should receive the appropriate proportion of the corresponding monetary award." See also page 28 of the *National Health Service*, by Ormrod, Harris Walker, and Ellison, under section 9, subsection 1 (b). As a direct consequence of this a consultant working part-time in the National Health Service receives only a proportion of his merit award.

If the foregoing assumptions are correct it would follow that professors who receive merit awards should be paid—as are other consultants—a proportion of their awards, represented by the proportion of their time devoted to the National Health Service. I mention these points because there exists an impression that professors—remote from the restrictions imposed on others—are to receive the total

emoluments of awards regardless of sessions worked. The last paragraph of your leading article appears to express an opinion consistent with this view. If such action be contemplated I should be glad to learn by what authority it is sought to override what appears to be the clearly expressed intention set forth in my first paragraphs. It will be observed that the (secret) honour is in no way affected, only the monetary award.—I am, etc.,

Sheffield. JOHN L. EDWARDS.

Potassium Permanganate as Abortifacient

SIR,—In the Croydon obstetric service during recent months we have observed about ten cases of painless severe vaginal haemorrhage due to the introduction of tablets of potassium permanganate into the vagina with intent to procure abortion. We have been unable to find any reference to this condition in the medical literature of this country, although the American and Continental journals contain many references[1 2 3] to the subject. The practice, however, appears to be on the increase since the war, and emphasis on the great dangers associated with it might serve a useful purpose.

It is obviously difficult to provide evidence of abortions achieved by this means, but it seems that a pregnancy is not disturbed unless the tablets are introduced high into the vagina in the neighbourhood of the cervix. Those cases seen in Croydon have had localized lesions on both anterior and posterior walls at about the junction of the lower and middle thirds of the vagina. There is frequently an attempt to mislead the clinician. The symptoms are of profuse, painless, and frequently continuous vaginal haemorrhage, associated with a period of amenorrhoea or an irregular menstrual cycle, and the condition is to be differentiated from threatened or inevitable abortion, and from other forms of criminal interference.

If the condition is not to be overlooked the physical examination of any such case must include inspection of both cervix and vagina in a good light, for usually the cervix is found to be closed and the haemorrhage, frequently arterial, can be discovered only on inspection. There may, of course, be an objection to any form of vaginal examination in the case of threatened miscarriage, on the grounds that the condition might be converted into an inevitable abortion, and one or two of our earlier cases were not diagnosed correctly until the bleeding had persisted for an unnecessarily long period of time. Naturally in some cases haemorrhage ceases spontaneously, but a catgut ligature is usually required and vaginal packing is unnecessary.

The lesion is localized on opposing walls, and presents superficial ulcers of the epithelium associated with the erosion of a vessel, frequently an arteriole. Covering the ulcer in the early stages is a brown slough consisting of oxidized tissue and oxides of manganese. Convalescence is usually uneventful, uncomplicated by secondary haemorrhage. We have seen no fatal case following the use of the tablet form of potassium permanganate.

Potassium permanganate is a strong oxidizing agent but a poor abortifacient. Its effect is rapid and usually localized to the site of contact. Jetter and Hunter[4] stress the potential danger of further corrosion from potassium hydroxide, which, as a strong alkali, would be able to penetrate deeper into the tissue. McDonough,[5] who reviewed 65 cases, found only six in which abortion followed the treatment. He also describes one case with such severe scarring of the posterior lip of the cervix that elective caesarean section was performed at term. Such deep scarring is probably the result of potassium hydroxide. Jetter and Hunter further describe the general effects of potassium permanganate in reporting a fatal case following attempted abortion with a douche of concentrated solution. The whole skin was coloured a light mahogany brown, and the post-mortem examination revealed extensive superficial haemorrhagic necrosis of the uterus, pigmented casts in the lower nephron, alkaline methaemoglobin in the serum, and evidence of acute intravascular haemolysis. Although no reference to anuria has yet been made, it must remain a possibility in any such case.

It is with pleasure that I acknowledge the help of Mr. A. F. Clift.

—I am, etc.,

Thornton Heath. J. C. MILLER.

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Pink Disease and Sweating

SIR,—May I support your editorial protest (February 17, p. 344) against attributing pink disease and other vague symptoms of ill-health in early childhood to suprarenal cortical insufficiency? Surely the great majority of the biochemical findings reported by Sir Stanton Hicks and Dr. D. Cheek (February 17, p. 317) can be explained by one of the most constant symptoms of the condition—namely, excessive sweating. Although sweating is mentioned in the text of Sir Stanton's paper, it does not appear in Tables II and III among the "Main Symptoms and Signs"; yet in my experience it is never absent. It would explain the haemoconcentration nearly always found, and it would also account for the subnormal plasma sodium.

Fifteen years ago (*Arch. Dis. Childh.*, 1936, **11**, 49) I brought forward evidence of intolerance to heat in pink disease. In the Midlands, at any rate, it is rare in the winter. (Apparently in Newcastle there is no seasonal incidence, but where coal is plentiful the temperature of the home is apt to be high.) A patient on being exposed to sunlight showed alarming toxic symptoms, while another accidentally exposed to sunlight through glass died the same day. Keeping the patient cool is, in my experience, the most valuable single therapeutic measure. I suggest that if the patient sweats he is worse, and if he can be stopped from sweating he is better.

The ingestion of salt may well have a similar effect. (Does the ingestion of large amounts of sodium chloride have any effect on sweating?) Personally, I have had insufficient experience of the treatment to form an opinion, but in the two cases in which I have used it the result was not impressive.

Sir Stanton Hicks mentions Jaudon's work on suprarenal insufficiency in early life, and admits that the syndrome described by him is utterly unlike pink disease. He also rightly gives hypertension as a constant finding. Surely this indicates increased rather than diminished suprarenal activity? Where so many of the symptoms and findings can be explained by the excessive sweating which is always present it seems unnecessary to accuse the fashionable suprarenal cortex of "hypo-function." (What a word!)—I am, etc.,

Leicester. J. VERNON BRAITHWAITE.

SIR,—On reading recent literature on the role of suprarenal dysfunction in the aetiology and treatment of rheumatoid arthritis, gout, acute rheumatism, and other collagen-tissue diseases, I have been driven to the impression that the long-suffering suprarenal glands are being overworked by students of aetiology. Admittedly, recent contributors to the literature have stated that the therapeutic benefit obtained from the use of A.C.T.H. and cortisone must be considered as non-specific and of doubtful relevance in aetiology. We are thankful for such a frank attempt to put the matter in the right perspective, but the article on the relationship of suprarenal hypofunction to pink disease (February 17, p. 317)—an article fairly criticized in subsequent pages—is again disquieting.

Surely the low plasma sodium can be explained by the loss of sodium chloride in the profuse sweating which is so characteristic of the disease? Further, how can the constant occurrence of hypertension be reconciled with a suprarenal *hypo*function? No doubt the suprarenals are

immature in early childhood, but so are the ovaries and testes. Why not blame them for the sweating, the erythema, and the irritability which remind us of the climacteric state in adult life? Furthermore, we do experience rare instances of fulminating infective disease (and pink disease may yet be an infective disease) in which grave suprarenal hypofunction ensues, but there we do not blame the suprarenals but the meningococcus or pneumococcus, as the case may be. Again, the beneficial effect of D.C.A. may merely be non-specific in that it causes salt retention, as it does in other conditions in which the role of the suprarenal in aetiology is considered equally equivocal.

Just as the pituitary has been nicknamed the Leader of the Endocrine Orchestra, the suprarenal is having the role of drum forced upon it, since it is mercilessly beaten whenever the occasion appears fitting.—I am, etc.,

London, S.W.14. J. T. H. KNIGHT.

Diseases of Maladaptation

SIR,—The rather clumsy phrase "diseases of adaptation," which has become popular lately as a synonym presumably for "maladaptation," seems redundant to a Darwinian. All disease is evidence of an organism's maladaptation to its environment. But a "disease of maladaptation" (see your leading article, February 10, p. 285) is incomprehensible to me, except as a disease of a disease. In this sense, perchance the alleged cure of cholera by the specific bacteriophage of *Vibrio cholerae*, or superparasitism in general, could be euphemistically termed "disease of maladaptation." But, frankly, I am puzzled.—I am, etc.,

Leamington Spa. SHELDON F. DUDLEY.

Vegetarianism

SIR,—Your annotation on the meat shortage (February 17, p. 347) includes the assurance that "robust health may readily be supported by vegetarian diets which include milk." The term vegetarianism is too well established to be displaced or replaced, but it is an unfortunate term. Fundamentally it means a diet exclusively of vegetable origin, and this in fact is the definition given in Dorland's *Medical Dictionary*. Stedman says that a strict vegetarian avoids tubers and everything except fruit and vegetables grown in the sunlight, but adds that a lacto-vegetarian eats tubers with eggs and anything except flesh foods. The *New Oxford Dictionary* defines vegetarianism as abstention from eating meat, fish, or other animal products, but alternatively as the practice of living wholly or principally upon vegetable foods, especially abstaining from animal food obtained by the direct destruction of life. There must be extraordinarily few human beings who comply with Dorland's or Stedman's first definitions; and as in common practice there is no avoidance of animal foods other than flesh—or shall we say food that has been obtained by slaughter?—the comparative merits of animal and vegetable proteins in nutrition are not easily assessed.

Some fifteen years ago, when investigating the dietetic habits of athletes, I observed that a certain number of prominent performers described themselves as "vegetarians," and their success was advanced as an argument against the carnivore. At that time there were, of course, no restrictions of any kind imposed by conditions of supply or, for that matter, economy. I append the daily dietary of a champion long-distance cyclist: 1 lb. of brown bread; 6 oz. of butter; 4 oz. of cheese; 3 eggs; 1½ pints of milk; 6 oz. of oatmeal with brown sugar; apples, grapes, oranges *ad lib*.

We may sympathize with prejudices founded on humanitarian or aesthetic grounds, but it would not appear that from the point of view of nutrition the practising vegetarian, in the usual sense of the word, is sacrificing very much, if anything. Whether or no some special virtue resides in the proteins of meat as compared with other proteins of animal origin, or whether sapidity alone is the chief advantage, it is difficult or impossible to say.—I am, etc.,

London, W.1. ADOLPHE ABRAHAMS.

Erythrocyte Sedimentation in Anaemia

SIR,—I am in entire agreement with Dr. Richard Terry's excellent argument (January 27, p. 189) against the so-called "correction for cell-volume" in the sedimentation rate. I have been opposing this on similar grounds for 20 years, and have frequently expressed my opinion accordingly (*Modern Diagnosis*, 1946; *Medical Diseases of the Locomotor System*, 1947, etc.).

Apart from the theoretical argument, it seems to me that the practical observations are conclusive. I have had in one of my hospital wards for the last four years a patient with aplastic anaemia who cannot be transfused on account of violent reactions that occur in spite of every precaution. Her haemoglobin has been in the vicinity of 30% for the greater part of the time, but her uncorrected sedimentation rate is invariably normal. In the face of such a case as this, the arguments in favour of correction for cell volume seem futile.—I am, etc.,

London, W.1. J. W. SHACKLE.

SIR,—Dr. R. Terry's article (December 9, 1950, p. 1296) on this subject has given rise to an interesting symposium in the columns of the *Journal* (December 23, 1950, p. 1445; January 27, p. 189) to which I wish to add some facts—and perhaps some fancies—from my personal experience.

To begin with well-established observations, it was repeatedly noticed by me and my associate, Dr. V. Bianchi, that in Mediterranean anaemia, especially in the so-called moderate form, the sedimentation rate (E.S.R.) was generally slower than normal, and the more so if "corrected" for the degree of the anaemia. With exchange experiments—viz., after thorough washing, etc., resuspending "Mediterranean" erythrocytes in normal plasmas, and vice versa, always maintaining the same haematocrit values—it could be demonstrated that these excessively thin, hypochromic, and flexible red corpuscles sedimented at a vastly slower rate than the normal ones, and that the rouleaux formation in the Westergren pipettes was definitely hindered. It was deemed safe to conclude that corpuscular factors were primarily responsible for the sluggish E.S.R. of moderate Mediterranean anaemia, causing a sort of flotation of the leptocytes typical of the disease. This effect grows less distinct with the increase of the anaemia, so that it is somewhat less evident in genuine Cooley's anaemia.

On the other hand, departing from Heilmeyer's remarkably clear description of the grossly increased E.S.R. in so-called idiopathic aplastic anaemia, my co-worker Dr. R. Cataldi and I have shown by the same interchange technique that both corpuscular *and* plasmatic factors were synergically responsible for the extremely high values seen in this disease. This is readily intelligible if one bears in mind the number of septic complications which are wont to take place in the aplastic condition, together with the striking medullary reticulosis and plasmacytosis, associated with hyperglobulinaemia, which generally replace haematopoietic bone marrow. Similar observations could be made, always in interchange experiments, in the anaemic variety of multiple myeloma.

All these researches were performed with the original Westergren technique, on which point I fully sympathize with Dr. Wright's remarks (December 23, 1950, p. 1445).

Should I be allowed to draw theoretical conclusions, I believe that both *corpuscular* and *plasmatic* factors should be considered in the E.S.R. of anaemia: the former are *numerical* and *morphological* in character, the latter too well known to be dealt with here. All these factors add together in algebraic fashion, so that the final result may be sometimes enhanced and sometimes diminished: *there exists no "ideal" anaemia*, and this is the chief reason for which Wintrobe and Landsberg pointed out already in 1935 that "methods of correction for the effects of anaemia are crude and artificial."

In common practice the reading of a greatly increased E.S.R. in a mild or moderate anaemic condition should lead to research into the underlying causes, as recently emphasized by Barbier and Piquet; while on the other hand retardation of the E.S.R. in a highly or moderately anaemic patient should be equally investigated. *Correction should not be performed on a diagram*, but in the mind of the "critical physician" (Wintrobe) who is evaluating the laboratory findings in his anaemic patient, including the erythrocyte sedimentation test.

Another point which, to my mind, would have deserved some attention, as particularly frequent in anaemia, is that peculiar phenomenon by which the usual clear-cut delimitation line

between the sedimenting corpuscles and the transparent plasma is replaced by a coarse granular pattern, which is, of course, the macroscopic equivalent of larger rouleaux formation This characteristic phenomenon, which grows qui.e outstanding in some cases of miscellaneous anaemias, has been tentatively explained by Gripwall (his so-called "Schleiersenkung") as the consequence of a spontaneous enrichment in reticulocytes, but that this is not a satisfactory explanation is shown by its frequency also outside the domain of haemolytic jaundice.

In my opinion the greatly increased aggregation of the red corpuscles, the reduced retarding effect of the medium, the alterations of the plasma, and the retardation of the packing phase all play a role in this often outstanding alteration of the erythrocyte sedimentation test in some cases of severe anaemia.

—I am, etc.,

Genova, Italy. ALBERTO MARMONT.

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SIR,—The article by Dr. R. Terry (December 9, 1950, p. 1296) and much of the correspondence which has followed it (January 27, p. 189) have to a certain extent been confused by a lack of appreciation of the factors involved in the sedimentation of red cells in their own plasma.

Arguing from first principles, one may commence with the general form of Stoke's law for infinite fluids, say:

$$M = \frac{\beta D^2(p_1 - p)g}{\alpha V} \qquad (1)$$

where

M = maximum velocity (where flow is viscous).
β = a constant concerned with the volume of the particle.
α = a constant concerned with the area of the particle.
p_1 = the density of the solid.
p = the density of the supporting fluid.
V = the viscosity of the supporting fluid.
D = the dimension of the particle.

In specific form—i.e., for spherical particles—$\frac{\beta}{\alpha}$ equals $\frac{1}{18}$ in ft. lb. sec. units, and $\frac{2}{9}$ in c.g.s. units.

By the use of this we have assumed that we are dealing with an infinite fluid, but in the case of blood sedimentation we are not; and the density and viscosity of the supporting fluid become greater immediately the cells start to fall. In other words, packing begins almost immediately. We should therefore rewrite equation (1) in differential form, thus:

$$\frac{dX}{d\theta} = \frac{\beta}{\alpha} D^2 \left(\frac{p_1 - p_x}{V_x}\right) \qquad (2)$$

where X is the height of the column of cells, θ is time.
p_x and V_x are functions of and therefore vary with X, thus:

$$p_x = \frac{\text{Mass of cells + Mass of plasma at X}}{\text{Volume at X}}$$

and

$$\log V_x = \log V_p (1 - H_x) + \log V_e H_x$$

where V_p and V_e are the viscosities of the cells and plasma respectively, and H is the relative volume occupied by the cells at height X.

If we were to plot the fall of the red cells against time until packing was apparently complete we would obtain a curve of sigmoid form such as is given by the formula

$$y = \frac{K}{1 + Ce^{rt}}$$

where t is time and K, C, and r are constants.

It is apparent that the rate of increase of density and of viscosity of the remaining column of cells will not be as rapid in an anaemic blood, and that therefore, *per se*, anaemia must have an effect on the maximum rate of sedimentation.

It will be noted here that I have specified the maximum rate of sedimentation, for this has an entirely different significance from the fall after a specified time such as one hour. This one hour may, and indeed occasionally does, bring us into the range of ultimate packing. In most cases, however, the maximum velocity of fall has not been reached within the one hour usually employed as a criterion.

The increase in sedimentation rate seen in various pathological conditions is probably mainly due to the adherence of one red cell to another, and in fact such cases are the best to use for the demonstration of rouleaux. When two cells adhere one to another, the ratio of volume to area becomes very different, particularly so when we are dealing with disk-like particles such as red cells, the adherence of two of which in rouleaux formation means almost a halving of the exposed area. It is small wonder then that such clumping of red cells gives rise to an increase in sedimentation rate. For this clumping to occur, however, the cells must contact one another, and the probability of collision becomes smaller the more anaemic the blood. Furthermore, anaemias are frequently associated with distorted red cells, and such cells are not able to adhere one to the other with the same loss of area. For example, two spheres sticking together would lose but little of their surface area, and the value $\frac{\beta}{\alpha}$ would be little changed.

Thus it would appear that in anaemia we have conflicting factors operating, and there are probably others than those I have mentioned. Fundamentally, therefore, correction based on tables worked out from diluted blood may be misleading, but on the other hand we cannot afford to neglect the effect of anaemia, and to this end I would recommend simultaneous reporting of the sedimentation rate together with the packed cell volume, which can conveniently be done by the use of Wintrobe's tubes.—I am, etc.,

Durban, S. Africa. R. ELSDON-DEW.

Physics of Breathing

SIR,—May I, as a physicist, rise in defence of Poiseuille's law as applied to the resistance of the trachea to respiration, and correct a few misconceptions put forward by your correspondent Mr. Halek (February 3, p. 246)? He states that the law holds only for tubes of capillary dimensions, but in fact the law can be applied to a tube of any size provided that the flow of gas through it is streamline. The upper limit of validity is determined by the transition to turbulent flow, and the lower limit by the tube diameter being so small as to be comparable with the mean free path of the gas molecules—much less than a thousandth of a millimetre, at atmospheric pressure.

He also states that the law holds only for incompressible fluids, which is true; but the elementary formula is very easily elaborated to be valid for gases which obey Boyle's law, pressure times volume being equal to a constant. Nevertheless, if the pressure differences involved are small compared with the atmospheric pressure (as they are in this case) there would be no serious error in applying the elementary Poiseuille formula. For the most accurate work there are small corrections to be made for effects taking place at the ends of the tube, and for the kinetic energy of the moving fluid, but they are, of course, of no significance here.

Going back to the paper by Mr. Jackson Rees (December 23, p. 1419), he does not appear to have considered the relative lengths of the infant and adult tracheas, and I would agree that the resistance to flow of the infant trachea is 256 times that of the adult only if the infant and adult tracheas were the same length. Surely the length of the infant's trachea would be only about one-quarter of the length of the adult's and the factor would then become 64.—I am, etc.,

London, W.14. J. A. W. HUGGILL.

Lubricant Unnecessary for Syringes

SIR,—The observation of Darling and Spencer (February 10, p. 300) that a silicone may be used in place of liquid paraffin as a lubricant for syringes which are to be sterilized by hot-air at 160° C. is useful to those concerned with the running of syringe services. We also, in this laboratory, became very dissatisfied with the disagreeable mess produced by liquid paraffin and wondered whether it was really necessary to use a lubricant at all. We were rather surprised to find that lubricants are indeed unnecessary in syringes, and for two years now we have prepared without lubricants all syringes used for intravenous work and the results have been entirely satisfactory, there having been only one complaint of a syringe with a plunger stuck in its barrel.

The syringes, which are all glass, are well washed in cold water in the ward or clinic immediately after use, and later, in the laboratory, they are washed again under the cold water tap. They are then rinsed first in distilled water, then in methylated spirit, and finally in ether. The last three cleansing fluids are placed in small beakers from which they are sucked up into the syringe and squirted back again, the process being repeated two or three times in each case.

It should be noted that neither soap nor hot water is used, and these appear to be unnecessary provided the syringes are well rinsed immediately after use.—I am, etc.,

Dartford, Kent. MALCOLM PEARSON.

Side-effects of Antibiotics

SIR,—I agree with Dr. W. Tomaszewski (February 24, p. 388) that, with the increasing use of chloramphenicol and "aureomycin," attention is focused more and more on the side-effects of these newer antibiotics. Since my report dealing with serious untoward effects of aureomycin was the first to appear (*British Medical Journal*, 1950, **1**, 491), and was subsequently followed by an annotation (ibid., 1950, **1**, 1184), I may perhaps be allowed to make some comments on this question.

The most dramatic manifestations besides diarrhoea, depression, and drowsiness are undoubtedly the changes of the mucous membranes. My colleague, who was the unfortunate subject of my original letter, will certainly agree with Dr. Tomaszewski that the side-effects may make the use of these antibiotics "somewhat difficult and unpleasant." As those patients entitled to obtain aureomycin in this country at present are usually seriously ill, it appears to be of considerable importance to spare them troublesome after-effects. Since my communication it appears to be agreed that the administration of vitamin-B complex is most efficacious both in prevention and for the treatment of these symptoms. It has been my practice during the last 13 months to give three tablets three times daily, starting simultaneously with the first dose of aureomycin, of a preparation containing 5 mg. thiamine, 2 mg. riboflavin, 20 mg. nicotinamide, 2 mg. pyridoxine, and 3 mg. calcium pantothenate. Untoward after-effects were not observed if B-complex was continuously given for at least one week after cessation of the aureomycin administration. Recently, however, in the case of a young house-surgeon who contracted a penicillin-resistant intranasal boil with facial cellulitis, administration of nine of the tablets daily did not prevent a moderate glossitis and stomatitis with very troublesome anal and perineal pruritus (total dose 5 g. aureomycin).

The explanation of the mechanism of these mucous membrane changes has not advanced substantially since my original report, but some additional partly controversial findings concerning aureomycin and vitamin B_{12} have just been discussed in the *Journal* (February 24, p. 404). It is also puzzling that 10–20 times the daily requirement of the B-complex vitamins should be necessary for the prevention, or alleviation, of untoward side-effects after only a short course of aureomycin treatment in otherwise well-nourished patients. Still, until more knowledge has been accumulated, it would save much additional suffering if patients having aureomycin and chloramphenicol treatment were routinely given large doses of vitamin-B complex.—I am, etc.,

London, W.1. Z. A. LEITNER.

Pethidine Sensitivity

SIR,—Dr. R. I. Bodman (February 17, p. 354) in his criticism of my case report (January 20, p. 125) elaborates the points raised by Dr. Harry F. Griffiths (February 3, p. 250), and I feel that some reply is necessary in order to put things in their proper perspective.

Considered stage by stage, the case takes on a different aspect from that represented by Dr. Bodman's telescoping of events. Some seven or eight minutes elapsed between the initial administration of thiopentone and the injection of pethidine; this time was taken up with intubation and the arrangement of the patient on the table. After intubation the patient began to breathe in a matter of seconds, and regular respiration was established within a minute or so. This was particularly remarked, as the case was being demonstrated to postgraduate students.

Dr. Bodman seems to suggest that, after the usual effects of thiopentone had been established for some minutes, it so happened that almost immediately after an injection of pethidine the thiopentone suddenly produced, as an afterthought so to speak, or perhaps because of some kink in the space-time continuum, profound hypotension. While not disputing that thiopentone can produce severe hypotension where cardiac disease exists, or when given in excessively large doses, I cannot accept that either of these conditions was present in the case under discussion. Indeed, Griffiths and Gillies (*Anaesthesia*, 1948, **3**, 134), describing their technique for total spinal block, state that the usual induction dose of thiopentone is 1 g., yet it has never been suggested that the hypotension produced in their cases was due to this drug and not to the spinal block.

Of the other phenomena under discussion, the tachycardia may have been caused by "flaxedil," but was more probably the normal physiological response to hypotension in accordance with Marey's law. Dr. Bodman agrees that the apnoea was certainly produced by pethidine, but I cannot accept his view that the reaction observed was within the normal limits for that dose in that patient.

The fundamental principle in anaesthesia, and especially in closed-circuit anaesthesia, is equilibrium. Because of friction the perfect mechanical system capable of perpetual motion does not exist. In anaesthesia the equivalent of friction is, broadly speaking, catabolism, first of the anaesthetic agent and secondly of the body's resources. These changes, being fairly gradual, the system may be considered in equilibrium over a short period of time, and analogy with Newton's first law of dynamics leads us to look for a sudden cause for any sudden change. I maintain that the intravenous injection of pethidine was the cause of the sudden hypotension and apnoea in this case.

In the words of William of Occam, "It is vain to do with more what can be done with fewer," and I suggest that the three phenomena observed can be attributed to the pethidine alone and do not need three different causes to be ascribed to them.—I am, etc.,

London, N.W.11. D. ZUCK.

Acute Tonsillitis

SIR,—General practitioners learn with surprise if not with vexation that sulphonamides are valueless in acute tonsillar infections (February 17, pp. 323, 326; March 3, p. 474). Before the sulphonamide era acute tonsillitis was a severe illness accompanied by fever (even rigors), profound toxaemia, rapid pulse, fall of blood pressure, general signs of relative peripheral failure (giving a clinical picture often indistinguishable from acute diphtheria), in addition to the usual local throat signs with which all doctors are familiar. The acute phase continued for about a week, after which resolution took place or peritonsillar abscess followed.

Untoward and common sequelae were acute otitis media; less often but not infrequent were acute mastoiditis. More remote and rarer effects were rheumatic fever, arthritis (septic), pleurisy, and even malignant endocarditis. The latter were encountered in the poorer and more crowded districts.

Since the advent of the sulphonamide era the clinical picture has changed. One to three days initiates the period of convalescence, and untoward effects are extremely rare. This is not to argue *post hoc propter hoc*, as during the same period one has noted that scarlet fever has become a benign disease. In scarlet fever one must also conclude that sulphonamides have not been standard or universal, but again one cannot seriously argue that the therapy has not removed the sting from puerperal fever (prior to the use of penicillin, etc.).

In perusing the account of cases in the *Journal* one finds no mention of the state of the pulse, blood pressure, peripheral circulation, and other criteria of toxaemia. Now these data are of much more importance in assessing the condition of the patient than the presence of temperature or haemolytic streptococci in tonsils and local signs.

In puerperal fever grave toxaemia may be present in the absence of raised temperature, or temperature may be raised only once in 24 hours, but other signs of toxaemia are present, rapid pulse and peripheral circulatory weakness, while clinical recovery has often taken place, even if the cervical swab is positive for haemolytic streptococci.

It is possible, even likely, that tonsillitis is now a less virulent infection than in the old days (of scarlet fever), but there are other criteria to be assessed.

In the presulphonamide era I encountered on the average a peritonsillar abscess once weekly, say, while otitis media was not infrequent and acute mastoiditis not very rare. During the sulphonamide era I encountered peritonsillar abscess once and acute mastoiditis once. The peritonsillar case had acute tonsillitis for four days before sulphonamide treatment could be given, and the mastoid had no treatment for the tonsillar infection.

Until more observation is done and more data are available I cannot believe that sulphonamide therapy is superfluous in acute tonsillitis.—I am, etc.,

Fraserburgh. J. MACLEOD.

Treatment of Naevi

SIR,—I agree with Dr. Cyril M. Ross (February 17, p. 356) and Dr. R. E. Bowers (January 20, p. 121) on the importance of Lister's observation that the majority of the most common type of cavernous angiomata disappear spontanously, leaving usually little scarring, by about the age of 5 or 6 (I would have said 7). Lister cites certain exceptions, and I would have added a very important one: that when a mucous membrane is involved disappearance spontaneously must be extremely rare. Dr. Ross's observation of his failed case falls into line with this.

I have found that the γ rays of radium leave absolutely no scar and considerably reduce the time of disappearance, much to the parents' satisfaction. Consequently I used to employ this for all cases on the face and neck, and when the angiomata were multiple used those on the body as controls. In the rare cases in which repetition of the treatment is necessary it should not be done until a year or at least six months have elapsed. In order to prevent an overzealous assistant breaking this rule, after seeing the patient at three weeks to determine the amount of reaction I used to give a definite appointment for six months later. Some untreated cases ulcerate spontaneously, especially if very extensive, and these will leave scarring. The best way to stop the ulceration is by very small doses of radium γ rays once a week, with the possible addition of penicillin cream. In some cases this may be sufficient to start rapid regression, otherwise adequate treatment is given in a month or six weeks. *X* rays seem to cause more pigmentation in the early stages, but I have seen few of the late results. I have seen it recommended that the *x*-ray dose should be repeated in six weeks or two months, but this is much too soon and often the original dose suffices.—I am, etc.,

Cobham, Surrey. N. S. FINZI.

Environment and Intelligence

SIR,—I would like to suggest to some graduate in search of a suitable subject for an M.D. thesis that he should make an assessment of the intelligence of children adopted into good middle-class homes. The majority of these children come from working-class households, and it would be interesting to see how they compare with their class-mates in intelligence. My casual and limited observations appear to indicate that they compare very favourably. Additional light upon the subject might be got from the results of the scholarship examinations held by education committees, which most children take at 11 years of age and which have one section devoted to intelligence testing.

The effect of environment upon children has been studied extensively in the United States by comparing identical twins living under different conditions. One of the fallacies of this comparison is that identical twins have often substantial differences in height, weight, liability to illness, temperament, and so on. The number of identical twins available for investigation is also very limited. It should be a simple matter to carry out the testing of adopted children in school without causing them any embarrassment, by spacing them out between controls. The listing of adopted children can readily be done by their class teachers.—I am, etc.,

Rotherham. J. M. WATT.

The South African Meeting

SIR,—Your leading article (February 17, p. 342) interested me very much, and I should not like the occasion to pass without comment. As you pointed out, the B.M.A., as a medical organization, would not even attempt to interfere with or criticize the policy of the South African Government, but at the same time it has not sacrificed principle for expediency.

An attitude such as this is what one expects from an organization of men and women who subscribe to the rules of professional conduct summarized in the Hippocratic code, and I think it is not unfair to expect such an attitude from most self-respecting people—professional or otherwise. It is from the ranks of such people that a country's Government is largely chosen, and thus the policy of a Government will surely be influenced to a large extent by the attitude of these people.

All this may seem somewhat irrelevant, but I intend it to be the preamble to an attempt to show that, if the Medical Association of South Africa—and incidentally other organizations of educated and responsible men in South Africa—had not in the past so readily sacrificed principle on the altar of expediency, the extreme form of racial discrimination practised in South Africa to-day would never have found such a rich medium for its dissemination and growth.

In May, 1944, a non-European medical student at the University of Capetown was suspended from the University pending an inquiry by the disciplinary committee of that institution. His "crime" was that he had attended an orthopaedic clinic at which white patients were being examined. The objection to his presence was not from the patients but from his white colleagues.

He was found "not guilty" and acquitted. At the time the incident evoked considerable comment from all parts of the country. A former dean and archdeacon of Bloemfontein wrote to the *South African Medical Journal* deploring the failure of an enlightened and scientific body such as a university to brush aside the prejudice of the less enlightened. One would have expected the medical profession to have taken a strong stand to maintain its principles on this occasion. However, the editorial comment of the *S.A.M.J.* (July 8, 1944) adopted an extremely non-committal attitude and gave no clear lead such as appears in your

columns last week. I have given the reference for those who wish to read the complete editorial, but to make my point here I shall quote some of the relevant passages.

Paragraph 2 commences: "Correspondents have urged us to 'state the principles at stake clearly in this *Journal*,' but we do not think that such a course is either necessary or desirable." The article goes on to say that it "presumes" that the members of the South African Medical Association "subscribe to the principles universally accepted by our profession—namely, that medicine knows no distinction of colour, or creed, or kind, or kin." Therefore, "We do not think any useful purpose will be served by discussing . . . in this *Journal* the points that Dean Hulme raises." In its concluding stages it says, "In this matter of the Colour Bar in Medicine our Association has not, as yet, taken up an attitude that supports, or conflicts with what may be called the liberal and conservative schools of thought in the Union."

Not long after this incident, non-European medical students at Capetown were asked to sign a document which officially prohibited them from attending any "class, clinic, lecture, operation, or post-mortem examination, on a white patient."

If to-day the Medical Association of South Africa feels that the colour policy of the South African Government will lead to the country's isolation from scientific and cultural intercourse with the rest of the world, it would be interesting to contrast their present-day attitude with that of the editorial I have quoted.

In the last world war we saw how medicine and science were prostituted to serve the inhuman plans of the Nazis, and I think we should bear this in mind when dealing with ideologies which discriminate on grounds of colour, creed, or race. The medical profession should be ever to the fore in upholding all that is righteous, and the B.M.A. should be proud of the stand it has taken in deciding not to take part in the proposed joint meeting at Johannesburg because of South Africa's racial discrimination.—I am, etc.,

Derby. RALPH A. A. R. LAWRENCE.

*** Dr. Lawrence informs us that he was himself the student who was suspended from the University in 1944.—ED., *B.M.J.*

POINTS FROM LETTERS

Allergy with Procaine Penicillin

Dr. F. E. LOEWY (London, W.1) writes: Dr. T. V. Humphrey's experience of an alarming allergic reaction after injection of this preparation (February 10, p. 299) deserves special attention. The cause in his case was most likely sensitivity to procaine, not infrequently met with also after local anaesthesia for dentistry, etc. Patients complain of palpitation, nausea, and faintness for some hours, and it is customary but unjustified to put the blame on a minute trace of adrenaline usually injected at the same time. . . . It is certainly advisable before giving procaine penicillin to inquire for unpleasant reactions after injections for tooth extractions, for fibrositis, or for local anaesthesia.

Research by General Practitioners

Dr. C. E. S. FLEMMING (Limpley Stoke) writes: In the *Journal* of February 24 (p. 415) there is a letter by Dr. G. G. Dawson regretting that the general practitioner's claim to research is not acknowledged. In the *Journal* of June 3, 1944 (p. 759), there is an article on this subject by me setting out this claim in some detail.

Corrections

The author of the paper "Side-effects of Chloramphenicol and Aureomycin" in our issue of February 24 (p. 388) is W. Tomaszewski, not T. Tomaszewski.

In the leading article "Occupation and Peptic Ulcer" (March 3, p. 463) line 18 of column 1, p. 464 should read ". . . from 0.03% at ages 20–25 . . ." and *not* 0.3% as printed.

Professor A. D. M. Greenfield (Belfast) writes: The post referred to by Professors Frazer and Huggett in their letter "Spens Awards for Professors" (March 3, p. 477) at the Queen's University of Belfast is a lectureship in physiology and not a lectureship in dental physiology as they stated.

Obituary

P. J. MACLEOD, O.B.E., M.B.

Dr. P. J. Macleod, medical superintendent of Bridge of Earn Hospital, Perthshire, died on February 15 in Dundee Royal Infirmary at the age of 54. During his tenure of office he had established and developed in Bridge of Earn a rehabilitation centre which, under his lively and enterprising guidance, is now of national and even international reputation.

Peter John Macleod, who was the son of an outstanding Lewis seaman, meant to be an engineer. He went straight from school into the Royal Artillery in 1914 and did not take up his medical studies until after the war. He graduated M.B., Ch.B. at Glasgow University in 1924 and then served as an assistant in Stornoway before joining the Highlands and Islands Service, first in Applecross, then in Carloway. He returned as an independent practitioner to Stornoway, where he was prominent in forming the Outer Isles Division of the B.M.A. Early in the second world war the Department of Health for Scotland decided to establish a rehabilitation unit for miners at the E.M.S. hospital in Gleneagles Hotel, and Macleod was put in charge. Shortly afterwards he joined the R.A.M.C., but was later released to resume his work at Gleneagles. The scope of the unit was extended to surgical and medical cases generally, and with the closure of the hospital at Gleneagles it was transferred to the emergency hospital at Bridge of Earn. There after extensive alterations some 120 beds were devoted to this purpose. The adaptation, equipment, and organization of this centre were entirely according to Macleod's planning, and the success he achieved is ample proof of his efficient administration.

Sir Andrew Davidson writes: Macleod's approach to the subject of rehabilitation was warmly humanistic, based on an intense desire to do the very best for each and every patient. He believed that the work of the hospital was not complete till the patient had derived the maximum degree of restoration to fitness. The rehabilitation centre was called the "fitness centre" because he felt that rehabilitation began long before the patient reached the stage of going to a special part of the hospital. Rehabilitation began in the earliest stages of the illness and continued throughout treatment and if necessary after active treatment was discontinued. The fitness centre was thus only a part of the rehabilitation process. To visit Bridge of Earn was to see how the inspiration of a leader uplifted and gladdened the disabled patient and infused him with zeal in his task of working himself back to fitness.

One of the secrets of Macleod's success was that first and foremost he was a general practitioner of medicine. He had experienced the loneliness and the responsibility of single-handed practice in a remote area and was able thereby to enrich his natural interest in people by getting down to the very roots of human life. In the town of Stornoway he has left his mark; his house there was a centre of warm-hearted hospitality to the stranger.

In 1949 Macleod, who had been awarded the O.B.E. four years before, visited the United States and Canada with a Rockefeller travelling scholarship for the study of his subject, and during his sojourn there he was in great demand for discussion groups, lectures, and even broadcasting on one of the networks. His interests

ranged far and wide outside his professional duties. He was prepared to discourse on all sorts of subjects—economic, religious, and social—with a peculiarly clear and sensitive analysis and appreciation of the complexities of human instinct, thought, and personality. He understood the outlook of the common man and could sympathize with it and interpret it in fluent and entertaining language. He had a rich store of instances from his personal experience and observation with which he could illuminate his talk. His knowledge of the Highlands—particularly the Western Highlands—was profound, and he was well known and beloved in Gaelic-speaking circles.

"P. J.," as he was affectionately known to his friends and even to those who were of brief acquaintanceship, was engaged in work on one of the growing points of medicine and would have in the fullness of time conveyed to the world the results of his work and experience. His death at an early age means that others will have to undertake that task; but his work is laid on sure foundations and will continue. To his wife and helpmate we extend our deepest sympathy.

At a memorial service held at Bridge of Earn Hospital, the Rev. T. B. Stewart Thomson, M.C., D.D., expressed the thoughts of members of the hospital board and staff in the following terms:

"Others may pay just tribute to Dr. Macleod's brilliant talents, his far-seeing planning, his service to King and country in both world wars, the honours (borne so modestly) bestowed upon him. He was indeed a great man, a pioneer in the task of setting others on their feet again, fitting them afresh to fight life's battles. Thousands of former patients, both here and at Gleneagles, will recall his memory with gratitude to-day. But we of this hospital think of him in a more intimate way. He was the head of our very large family—surgeons and doctors, nurses, orderlies, administrators, and technicians, working men and women of every kind. He knew them all, was deeply interested in the part each severally had to play within this very intricate organization, often encouraging them with a kindly joke, an apt word, a passing smile. Never was there so harmonious a team, for never was there so magnetic a leader."

Dr. A. J. Macleod writes: Peter Macleod joined the Ross mountain battery of the Royal Artillery in 1914 from school. With this extraordinary unit, composed mainly of hillmen from Wester Ross and secondary schoolboys from Lewis and whose *esprit de corps* was fanatical, he served throughout the war, in the ranks of a somewhat rankless unit. His gift for the mechanical was used in the field to modify standard equipment for temporary needs. On one occasion a battery of an adjoining division had, under heavy bombardment, taken cover. Macleod, reaching them by a heavily enfiladed approach, stimulated them back to their guns, where in the course of the day they gained praise. It never occurred to anyone that the eager young man in worn but clean shorts was an ordinary gunner and not a staff officer. On another occasion, in a direct duel at deadly range, the gun on which he was layer silenced in turn three guns of an enemy battery. These incidents were a key to his being—a genius for encouragement and a craving for mechanical perfection. At the end of the war he decided to devote himself to "a piece of engineering worth while"—the human body.

The vast Glasgow Medical School of that time, with its unsparing clash of personalities, was certainly a school for thought. In it he sought not distinction but knowledge, and the historic figures of the day influenced him less than did one of the less prominent physicians, the late Dr. W. K. Anderson, whose main passion was to get the patient well. In all places, with intense spontaneous sympathy and sometimes feminine tenderness, Macleod lifted up the sick, encouraged or drove them to recover, and always strove to perfect means to that end. He drove himself unsparingly, sometimes beyond the danger point. He was the first general practitioner to be chosen as an examiner for the final M.B. at Aberdeen. Tall, lithe, with an olive, oval, latterly aquiline face, he was not a games man, but in a physical struggle he produced tremendous force and resistance. He controlled his superiors with ease. To the pompous he was studiedly casual or, if need be, sardonically rude; to all others he was unaffectedly charming.

Dr. JOHN WARE, honorary consultant physician to the Barrow and Furness Hospital Management Committee, died after a short illness on January 1 in the North Lonsdale Hospital, which he had served so faithfully and so well. The son of an architect, he used to say that he was born within the sound of Bow bells. He was educated at the City of London School and Caius College, Cambridge, where he gained first-class honours in the classical tripos. After leaving Cambridge he was for a period classics master at Loretto School. His thoughts later turned to the study of medicine, and he graduated M.B., Ch.B. at Edinburgh in 1908, proceeding M.D. in 1927. His thesis was most unusual, a translation of Galen on fevers. While at Cambridge he attained distinction as an oar, and at Edinburgh was captain of, and later coach to, the rowing club. John Ware was house-physician to the late Dr. Byron Bramwell; from him he acquired many of the habits and characteristics of that truly great master, and, as he often said, these were an inspiration in his practice of medicine. He came to Barrow-in-Furness in 1913, in partnership with Drs. Carmichael and Allan. Later the partnership became that of Ware, Carson, and Liddle. He was appointed the first honorary physician to the North Lonsdale Hospital in 1928, a post he held until 1945, when he also retired from his partnership. During the recent world war and after he was responsible for the local blood bank, and this worked with the greatest possible efficiency. Ware had a profound knowledge of medicine, which earned him the respect of all who came in contact with him. A superb physician, he was in fact a born teacher and might well have graced a university chair. This trait in his character found expression in the meetings of the local clinical society, of which he was chairman for many years. He had a kindly courteous nature and a subtle wit. A man of few words, all of infinite value, he was a staunch friend and a wonderful colleague. He leaves a widow and three daughters to mourn his loss, which is shared by a multitude of grateful friends and patients.

Dr. HENRY STEELE DEWAR died at Burnham-on-Sea on January 10, at the early age of 34. A native of Edinburgh, he was educated at George Heriot's School in that city, and went on to the university there, where he graduated M.B., Ch.B. in 1941. After house appointments at the Mental Hospital, Inverness, and the Royal Sussex County Hospital, he had spells as assistant in general practice at Enfield and Anstruther, Fife. Although in poor health, and knowing full well that it would take heavy toll of his strength, he deliberately chose general practice as his life's work, feeling that here was his true vocation. He went to Dorchester in 1945, and by his skill, his devotion to his work, and his genuine interest in all their problems he quickly endeared himself to his patients. Although so young, Dr. Dewar was a real family doctor. His smile and his sense of fun will always be remembered by those who knew him as a

colleague or a friend. His courage and patience in his long illness were an example to us all. Deep sympathy will be felt for his wife and two young children.—J. D.

Dr. J. A. R. SELBY, who was for 20 years in the Colonial Medical Service in Hong Kong, died at Cheadle Hulme, Cheshire, on February 15. He was born at Port William, Wigtownshire, in 1900, and was educated at Port William Public School, George Watson's College, Edinburgh, and Edinburgh University, where he graduated M.B., Ch.B. in 1925. He represented Scotland at rugby football in 1920. After qualifying, Dr. Selby held appointments at the Bradford Royal Infirmary, the East Pilton Hospital, and the Royal Infirmary, Edinburgh, and at St. Paul's Hospital, London. In 1930 he joined the Colonial Medical Service and went to Hong Kong, where he became medical officer. He was later promoted to health officer (social hygiene) in the medical department. He remained in Hong Kong until 1950. During the Japanese occupation of Hong Kong, from 1941 to 1945, Dr. Selby was interned in Stanley Camp. Five years later, in 1950, he retired from the Colonial Medical Service and returned to England, where he was appointed consultant venereologist for Stockport and East Cheshire. Our sympathy is extended to his widow and two sons.

Dr. JOSIAH ROWLAND BENJAMIN DOBSON died after a long illness patiently borne at the Finchley Memorial Hospital, Finchley, on February 22, aged 69. He was born at Cardiff in 1881, and was educated at University College, Cardiff, and St. Bartholomew's Hospital, London, where he qualified in 1909. Three years later he graduated M.B., B.S. (London). After holding resident posts at the Royal Hamadryad Seamen's Hospital, Cardiff, the South Devon and East Cornwall Hospital, Plymouth, the Royal Chest Hospital, London, and the Salterley Grange Sanatorium and Tuberculosis Dispensary, Birmingham, he was appointed tuberculosis officer to the Middlesex County Council in 1913. During the first world war Dobson served in the R.A.M.C. in the Mediterranean area, East Africa, and France, and in 1918 the French Government awarded him the *Médaille de Sauvetage en Argent* for saving life at sea. He was honorary secretary of the Tuberculosis Section of the B.M.A. when the Association held its Annual Meeting at Manchester in 1929. The North London Medical Society appointed him its president for a term, and he was also chairman of the Finchley Division of the B.M.A. in 1932–3. After he retired, Dobson occupied himself with his favourite pursuits of golf, fishing, and gardening, but last autumn failing health caused him to give up all forms of physical activity. He is survived by his son, now serving in the Australian Army, and by a grandson, the child of his deceased elder son.

Dr. Alfred Cox writes: The obituary notice of Dr. R. G. McGowan (March 3, p. 478) would have pleased its subject had he been able to read it. It was obviously written by one who knew McGowan intimately and shared his preference for plain and direct statement with "no frills." As I owed much to McGowan's co-operation during my term of office I should like to pay my tribute to his memory. The masterful way in which he handled his colleagues was a perpetual marvel and delight to me. His methods would not have suited in some areas, but the Manchester men trusted him implicitly and cheerfully submitted to the iron hand not often covered by the velvet glove, and McGowan gloried in their devotion to him, though he would never have described his emotions in such terms. The Association has lost a grand worker, whose secretarial record is unlikely ever to be surpassed. I treasure the memory of a sterling "character" and a "faithful" friend, who in his dealings with Headquarters was always candour itself, but always helpful.

Medico-Legal

NATIONALIZATION AND CHARITY

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

Lady Bland-Sutton, who died in 1943, left a substantial fund on trust to be applied for the benefit of the Bland-Sutton Institute of Pathology of the Middlesex Hospital. She stipulated, however, that if the hospital should become nationalized or by any means pass into public ownership the whole fund should go to the Royal College of Surgeons absolutely. After the National Health Service Act came into force the trustee asked the court for a ruling.

Mr. Justice Danckwerts, who heard the motion, held[1] that, because under the Act the property held by a medical school is vested not in the Minister but in the board of governors, neither the property nor the governing body is nationalized or passes into public ownership. He said, therefore, that, although in a popular sense the hospital was nationalized, the institute and its work continued in existence and the trustee might lawfully continue to apply the income of the endowment fund for its purposes. He also considered the question whether, if he were wrong on that point, the Royal College of Surgeons could take the "gift over."

As under the will the events determining the transfer of the fund from the purposes of the institute to the College could take place at any time in the future, however remote, the rule of equity known as the "rule against perpetuities" was offended unless the College was a charity in the legal sense. In 1899 the Court of Appeal decided it was not a charity, because one of its main objects was to promote the professional interests of surgeons as opposed to the public interest. Mr. Justice Danckwerts, however, held that he was not bound by the earlier decision, for it concerned only a particular statute and was directed to the quite different question of liability to taxation. He took the view that surgery needs for its practice a competent body of practitioners, and that the real object of the College is the promotion and encouragement of the art and science of surgery and not the interests of surgeons.

The Court of Appeal, which considered the case on February 2, overruled[2] the trial judge on both those points, but their reversal of his judgment makes no difference at all to its result. The Lords Justices held that the hospital had been nationalized even though the medical school and the institute remained free from national ownership and control, and that therefore the gift over would take effect if the College were a charity. But on this point they ruled that they were bound by the Court's earlier decision and that there was no evidence on which they could find, without untenable refinements, that any selfish professional purpose of the College was only ancillary to its charitable purpose. Therefore, they said, the gift over was bad. This, however, does not mean that the money goes to the persons who would be entitled to take it if there had been no will. An old rule of equity, the rule in *Lassence* v. *Tierney*, operates in a case like this to preserve the original gift. Hence, even though the Middlesex Hospital has been nationalized, the proceeds of the fund still go to the Bland-Sutton Institute. As the institute itself remains largely independent, the real intention of Lady Bland-Sutton is substantially carried out.

At the time Mr. Justice Danckwerts was trying that case at first instance, his learned brother Mr. Justice Wynn Parry was concerned with a somewhat similar one.[3] The testator had left £6,000 to the Fleet and District Hospital (near Farnham, Surrey) if it were still at his death run on the voluntary system and not taken over by the State. The residue of his estate he left to the same hospital "for

1 *British Medical Journal*, September 16, 1950, p. 685.
2 *Re* Bland-Sutton Will Trusts, *The Times*, February 3.
3 *Re* Frere, decd. *The Times*, July 8, 1950.
4 *In re* Dean's Trusts (1950, 66 *The Times* L.R., Part I, 728).

endowment purposes." When he died the hospital had already been nationalized and so the legacy failed, but the court had to decide whether the disposal of the residue (including the £6,000) also failed because of the nationalization of the hospital although there was no specific condition in the will to this effect. On the one hand there was no apparent justification for reading the condition attached to the legacy into the gift of the residue. On the other hand, the testator had clearly indicated an intention that, if the hospital were taken over by the State, it should no longer be regarded as a charity. The gift "for endowment purposes" failed if the object were no longer charitable. However, the judge pointed out, Section 59 of the National Health Service Act empowers committees and boards to accept gifts, and the Court has recently held in effect[4] that a hospital does not cease to be a charity because of the operation of the Act. He therefore felt bound to hold that the will contained a good charitable disposition of the residuary estate. The testator's intention was therefore defeated because he failed to bind his gift of the residue with the condition he had attached to the legacy.

Medical Notes in Parliament

Smoke Pollution

On February 27 Mr. ANTHONY GREENWOOD raised the matter of smoke pollution, pointing out that smoke and grit reduced effective sunshine and raised the mortality rate of respiratory diseases and might also be a cause of cancer of the lung. He asked whether enough dust extractors were being made for industry and whether the National Coal Board was establishing low-temperature carbonization plants to produce smokeless fuel. He wondered whether enough was being done to educate both industry and public in the importance of clean air.

Mr. WILLIAM PALING drew attention to the problem of burning slag heaps. During the war when fires attracted enemy aeroplanes these heaps had been extinguished, but now they were burning once again, and it was almost impossible to live in comfort in their vicinity.

Mr. GEORGE THOMAS pointed out that if a man leaves his wireless on and thereby creates a public nuisance he can be restrained, whereas someone producing smoke, which is a far more evil nuisance, was apparently unrestricted.

Mr. G. S. LINDGREN, in reply on behalf of the Ministry of Local Government and Planning, said that the Ministry of Fuel and Power had produced a whole series of booklets and pamphlets, including a stokers' manual, to teach the avoidance of smoke. The Public Health Act, 1936, provided some legal machinery for preventing smoke nuisances, and local authorities were taking the matter very seriously. Coventry had a smokeless zone in operation and Manchester was to start one in 1952. Their establishment depended, of course, upon the planning of the area. Industry in general was being very co-operative, and efforts were being made to produce more of the necessary machinery. It was hoped that domestic pollution would be less on the new housing estates, where, in co-operation with the Ministry of Fuel and Power, some solid fuel appliances had been approved.

Medical Examination of Reservists

On March 1 Mr. J. A. BOYD-CARPENTER moved an amendment to the Reserve and Auxiliary Forces Bill to provide that a man might have at least 14 days' notice of the date of his medical examination. He pointed out that as the Bill stood there was no specified interval between the service of the notice and the date for reporting to the medical board. In earlier debate the Secretary of State for Air had said that seven days' notice would be allowed. He said that many civilian occupations—for example, commercial travellers and proprietors of small one-man businesses—might find it difficult or impossible to arrange in the time to attend one of the 93 medical boards in the United Kingdom.

Mr. FREDERICK LEE said that in actual fact a man could state that the day proposed for his medical examination was inconvenient because of business arrangements and the date could then be changed.

Mr. BOYD-CARPENTER asked whether the notice for the medical board stated that a man could get the date changed if it was inconvenient.

Mr. LEE said that he could not answer this, but in the far bigger task with National Service men no problems had arisen. It would be difficult to give so much time between notice and date of board in the case of those men due to be called up at the end of April.

Mr. MANNINGHAM-BULLER asked if it was the intention of the Ministry of Labour sometimes to give less than 14 days' notice.

Mr. J. GRIMOND said that the penalty of £25 for non-appearance was worrying him in these circumstances.

Dr. BARNET STROSS suggested that a medical examination was altogether unnecessary since the men in question were all fit not long ago, were not going into active service or out of the country, and were not likely to have a particularly arduous training. Territorials going to camp did not always have a careful examination.

Mr. LEE said he could not accept this rather revolutionary suggestion, because if fatalities occurred the Government would be in a most indivious position. They were dealing with an older type of man than those usually in the Territorials.

The amendment was by leave withdrawn.

On March 5 Mr. J. A. BOYD-CARPENTER moved a new amendment to provide that no one should be convicted by a court for non-attendance at medical examination on the date specified in the notice if the time of warning is unreasonably short. He said this replaced his earlier amendment, imposed no time limit, but was designed to prevent injustice. The amendment was supported by Mr. A. J. IRVINE.

Mr. MICHAEL STEWART accepted the amendment on behalf of the Government.

Inoculations in the R.A.F.

Mr. P. WELLS asked on March 2 for information about the new inoculations in the R.A.F.

Mr. A. HENDERSON replied that a combination of two well-tried immunizing agents, T.A.B. vaccine and antitetanus toxoid, was being given under the name T.A.B.T. Two injections were given initially, a few weeks apart, and one injection annually thereafter or on first arriving overseas. All ranks were periodically reminded that vaccination and all inoculations were voluntary.

Money for the Health Service

In the Civil Estimates for 1951–2 the Ministry of Health is to receive £1.23m. and the Department of Health for Scotland £0.62m.; the National Health Service is to receive £120m., with an additional £14.35m. for its work in Scotland.

Payment of Chemists.—About £3.5m. was owing to chemists on January 31 last, representing nine-months' arrears in payment. A staff of 1,015 was engaged in pricing.

Hospital Costs.—A uniform system for analysing hospital costs in detail has been introduced for the first time this year and will relate to 1950–1 as a whole.

School Dentists.—At the end of last year there were the equivalent of 717 full-time school dental officers for 5¼ million pupils.

Allowances to N.H.S. Committee Members.—The maximum for loss of earnings or additional payments for members of hospital authorities, executive councils, and certain other bodies

in the National Health Service is 20s. a day. The comparable allowance for members of Ministry of Labour and Ministry of National Insurance committees is 25s.

N.H.S. Administration.—The total numbers of officers in the higher clerical, clerical, and general divisions on the staffs of hospitals were 14,589 on December 31, 1948, and 17,373 on December 31, 1949, the only dates for which figures are available.

Cost of Day Nurseries.—Gross cost for the year 1947–8 has been estimated at £3.5m. and the sums recovered by charges at £0.7m. Estimated average gross cost per child per week for the year 1947–8 was £2 11s. 5d. in the London area and £2 2s. 7d. elsewhere in England and Wales. The estimated average weekly charge per child was 9s. 6d. in the London area and 8s. 9d. elsewhere.

Smallpox.—The numbers of deaths in the five years 1946–50 were respectively 14, 15, nil, 5, and 1. The numbers of these cases in which there was information that the person had been vaccinated in earlier life were respectively 3, 6, nil, 1, and 1.

Universities and Colleges

UNIVERSITY OF OXFORD

In Congregation on February 24 the degree of D.M. was conferred on R. W. Parnell and Sheila R. Tangye.

UNIVERSITY OF CAMBRIDGE

In Congregation on March 3 a bequest to the University by the late Dr. C. M. Stevenson of the sum of £2,000 for the provision of an annual postgraduate prize in economics was gratefully accepted.

Professor Henry Albert Harris will retire from the Professorship of Anatomy on October 1. A meeting of the Electors to the Professorship will be held on April 19. Applications for the post should reach the Registrary, Old Schools, Cambridge, by April 5.

In Congregation on February 9 the following medical degrees were conferred:

M.D.—*J. A. R. Miles, *J. P. Bull, C. H. C. Upjohn, J. A. Cosh, J. Vallance-Owen, K. M. Hay, E. G. Sita-Lumsden, M. M. Bull, C. A. de Candole, R. Hodkinson.

M.B., B.CHIR.—*C. D. Lacey, *W. R. Juckes, *I. M. Guiver, *G. E. Sayce, *H. F. W. Pribram, *Vera Armett, *Rosemary A. Cooper, K. G. P. Mackenzie.

*By proxy.

UNIVERSITY OF LONDON

The King's College Hospital Medical School announces that the Sir Charlton Briscoe Research Prize and the John Everidge Research Fund in Urology were established last year. Sir Charlton Briscoe, who was honorary physician to King's College Hospital from 1908 until he retired from the active staff in June, 1935, is now consulting physician to the hospital and Emeritus Lecturer in Medicine to the medical school. Mr. John Everidge is a Fellow of King's College and consulting urological surgeon to King's College Hospital and a former lecturer in the medical school. He has been a member of the staff of King's College Hospital since 1919.

The Sir Charlton Briscoe Research Prize Fund consists of an investment of £1,000, the income from which is to be used for the encouragement of original research for the advancement of knowledge in any branch of medical science, and especially for work leading to the relief of pain and suffering in the sick. The income (approximately £30 per annum at the present time) is available for award to any member or members of the medical or dental staff of the hospital or medical school, or to any students or former students of the school. The object of the fund is to give some reward for research, interpreted in the widest sense, carried out or completed during the preceding year, which in the opinion of the committee is worthy of such recognition. The committee is appointed by the academic board of the medical school and consists of a senior physician, a senior surgeon, and a senior gynaecologist, with power to co-opt any individuals with special knowledge of the subject under consideration. The committee will not make any award unless it considers that work of a sufficiently high quality relative to the standing of the author is produced. In any year in which an award is not made the income for that year will be added to the capital fund.

The John Everidge Research Fund in Urology was established by Mr. John Everidge and is derived from the balance of the Windover Bequest, some £2,050, which was left to the urological department of the hospital, and a personal gift of approximately £450 from Mr. Everidge. The object of the fund is to provide financial assistance for the advancement of knowledge in genito-urinary surgery and ancillary subjects, particularly research likely to enhance the diagnosis and therapy of diseases of this system. The conditions of the fund provide that an award may be made for an essay or lecture reporting the objects or outcome of the research. It is open to all workers in this field, whether medically qualified or not.

Full particulars of both the prize and the fund may be obtained from the Dean, King's College Hospital Medical School, Denmark Hill, London, S.E.5.

UNIVERSITY OF MANCHESTER

The celebration of the centenary of Owens College, the first college of the Victoria University, will take place during the week beginning May 28 and will include a service in the Cathedral on May 29, when the address will be given by the Archbishop of York, and a reception in the Town Hall by the Lord Mayor and Corporation on May 30. On May 31 the Queen will attend a Congregation to receive the honorary degree of LL.D. The same honorary degree will be conferred also on Sir John Stopford, M.D., F.R.C.P., F.R.S., Vice-chancellor of the University since 1934.

Morris Markowe, M.D., D.P.H., D.P.M., has been appointed Lecturer in Psychiatry.

UNIVERSITY OF LEEDS

The following appointments are announced: *Senior Lecturer in Preventive Medicine and Public Health*, Robert Sutherland, M.D., D.P.H.; *Lecturer in Paediatrics and Child Health*, M. F. G. Buchanan, M.B., Ch.B., M.R.C.P.Ed., D.C.H.; *Lecturer in Clinical Dental Surgery*, R. T. Heylings, M.B., Ch.B., B.Ch.D., L.D.S.

Vital Statistics

Deaths from Tetanus

Drs. Conybeare and Logan discuss at page 504 various statistics of deaths from tetanus in England and Wales. The seasonal incidence of deaths from tetanus in 1939–48 is shown for England and Wales in the Table below. The figures for deaths in each month are taken from the Registrar-General's *Annual Reviews* for the years in question.

Deaths from Tetanus by Months in 1939–48, England and Wales. Civilians Only

	Jan.	Feb.	March	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Total
1939 ..	8	8	4	12	4	11	6	5	10	9	5	13	95
1940 ..	5	4	5	12	8	13	13	13	5	9	10	13	110
1941 ..	4	3	11	11	9	12	16	11	5	4	4	6	96
1942 ..	4	4	6	14	6	9	11	8	12	9	6	4	93
1943 ..	9	1	9	5	10	6	7	12	8	5	10	3	85
1944 ..	1	9	6	8	10	3	14	8	4	10	8	8	89
1945 ..	5	6	7	10	9	6	7	10	7	6	3	3	79
1946 ..	5	5	4	7	6	6	7	6	3	5	4	4	62
1947 ..	6	2	3	4	8	7	8	10	5	9	5	5	72
1948 ..	4	4	9	6	4	5	10	9	6	3	5	5	70
Total ..	51	46	64	89	74	78	99	92	65	69	60	64	851
Adjusted monthly totals ..	50	50	63	90	73	79	97	90	66	68	61	63	850
Adjusted monthly percentages ..	5·9	5·9	7·4	10·6	8·6	9·3	11·4	10·6	7·8	8·0	7·2	7·4	100·1

This Table excludes deaths of non-civilian males on and after September 3, 1939, and non-civilian females on and after June 1, 1941.

Below the figures for total number of deaths in each month during the 10 years are given adjusted monthly totals. The

adjustment has been made to eliminate the effect of the varying lengths of the months. The bottom row of the table shows the percentages of deaths occurring in each month calculated from the adjusted monthly totals.

There is clearly a seasonal incidence of deaths from tetanus, the months of April, July, and August showing notably high figures. The distribution of the monthly totals departs significantly from what would be expected if the deaths were distributed evenly throughout the months ($\chi^2 = 36.84$. $P < 0.01$). The high figures for July and August are possibly due to the fact that many people are then on holiday in country districts, as well as to agricultural activities at that time. The peak in April is more difficult to account for. That month is a particularly active one for gardeners, for much seed-sowing is done then. In recent years the first and second quarters of the year have shown higher numbers of births than the other two quarters, but the numbers of cases of neonatal tetanus are probably too small to account for the peak.

Influenza

In England and Wales during the week ending February 24 there was a continued and marked decrease in the influenza death rate in the great towns from 23.7 to 15.3 per million. The numbers of deaths decreased everywhere except for slight increases in the Northern and Eastern regions. The proportion of influenza deaths in the great towns in the age groups of 55 years and over was 89.3% compared with 88.8% in the preceding week.

In the great towns the following cases of and deaths from pneumonia, and deaths from influenza, have been reported:

	6/1	13/1	20/1	27/1	3/2	10/2	17/2	24/2
Pneumonia:								
Cases ..	956	1,300	1,455	1,702	1,664	1,515	1,002	853
Deaths ..	770	982	843	790	830	662	535	434
Influenza:								
Deaths ..	458	890	1,099	1,239	1,269	865	492	317

The deaths cannot be related to the cases in this Table.

Poliomyelitis

In the week ending February 24 notifications of poliomyelitis were as follows: paralytic, 16 (18); non-paralytic, 5 (6); total, 21 (24). The figures for the previous week are in parentheses. Total uncorrected notifications for the first eight weeks of the following years were as follows: 1947, 89; 1948, 316; 1949, 168; 1950, 367; 1951, 242.

Infectious Diseases

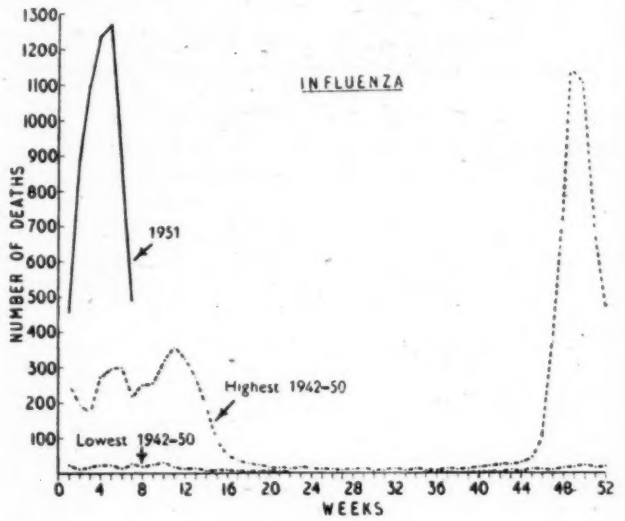
The chief features of the returns of infectious diseases in England and Wales during the week ending February 17 were increases in the notifications of whooping-cough and measles and a decrease in the notifications of pneumonia. The notifications of whooping-cough (5,662) were 552 above the record high returns of the preceding week. An increase was recorded in the incidence of whooping-cough throughout the country except in the North. The combined total for the North-western counties, Yorkshire, and the Northern counties was 56 below the total of the previous week.

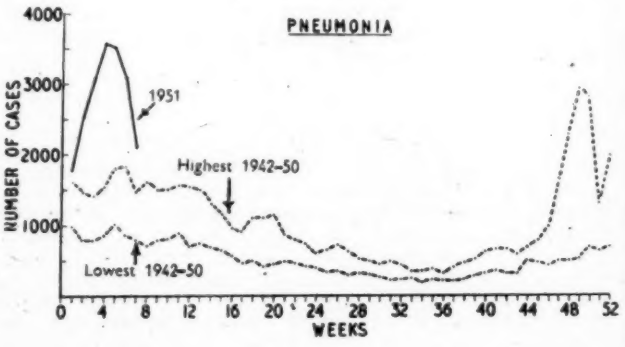
An increase of 2,952 in the notifications of measles (from 21,633 to 24,585) brought the incidence of this disease to the highest level recorded except for the 10th to 12th weeks of 1945. The rise in incidence during the week continued to be concentrated in London and the surrounding counties. The largest increases were Surrey 414, London 249, Middlesex 220, Kent 200, Lancashire 198, Essex 174, Yorkshire West Riding 148, Hertfordshire 130.

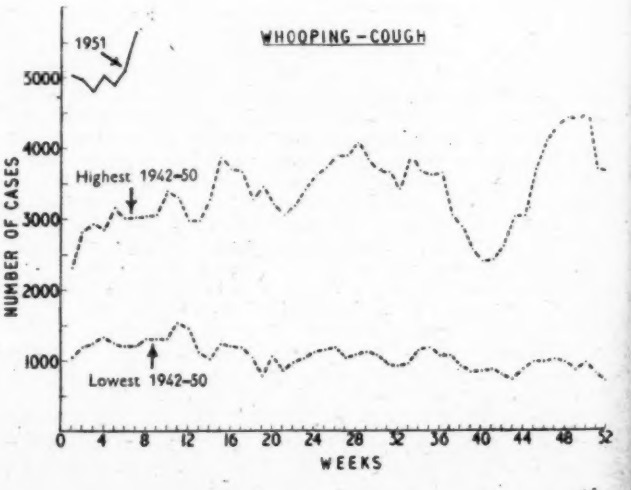
The largest variations in the returns of diphtheria were a fall of 7 in Durham and a rise of 4 in London. A fall in the incidence of acute pneumonia was reported from every area of the country and the notifications were 976 fewer than in the preceding week. Of the 10 cases of paratyphoid fever, 5 were notified in Kent, Swale R.D. The only administrative areas with more than one case of acute poliomyelitis were Birmingham C.B. 3 and Leicester C.B. 2. For the second consecutive week there was a large fall, 372 (from 864 to 492), in the number of deaths from influenza in the great towns.

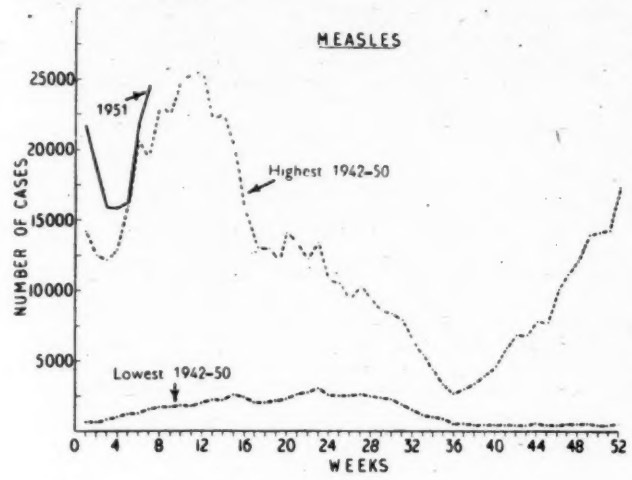
Graphs of Infectious Diseases

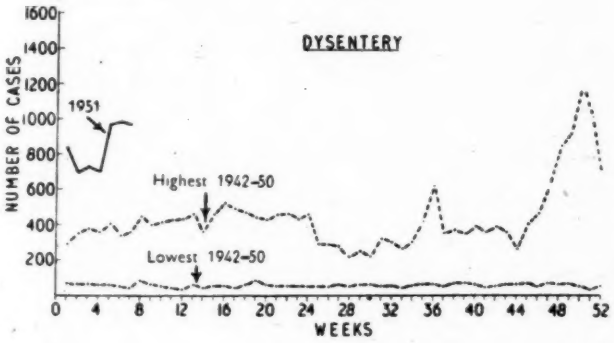
The graphs below show the uncorrected numbers of cases (deaths from influenza) of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1942–50 are shown thus - - - - - - -, the figures for 1951 thus ————. Except for the curves showing notifications in 1951, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.

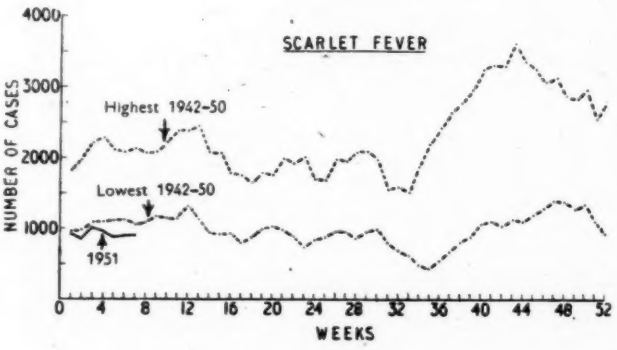












Dysentery

The incidence of dysentery continued at a very high level. There were 972 cases—only 13 fewer than in the previous week. During the first seven weeks of this year 5,889 cases of dysentery have been notified, while the annual totals were only 4,179 in 1947, 5,587 in 1948, and 4,819 in 1949. From the available evidence it appears that about 95% of the cases notified in the past year are Sonne dysentery and the remainder are mainly of the Flexner type. During the week the chief features of the returns were a new outbreak with 61 notifications in Dorset, Shaftesbury R.D., and an increase of 39 in the outbreak in Essex, East Ham C.B.

Low Diphtheria Incidence in Scotland

According to the Department of Health for Scotland there were only three deaths from diphtheria in Scotland last year—by far the lowest number ever recorded. In 1941, at the beginning of the immunization campaign, the number was over 500. The number of new cases last year, estimated at 150, was also a new low record. There were 333 notifications in 1949 and 12,395 in 1941. The number of children immunized is still not satisfactory. The number of pre-school children immunized last year remained fairly steady and was estimated at about 64% of the possible. But figures for children of school age immunized dropped from about 75% in 1946 to 62% last year. The latter figure is provisional and will be higher when all the returns are made.

1949 Outbreak of Cowpox

Cowpox in man probably occurs more often than is known, for it is not notifiable and is usually a mild disease. Drs. E. Donaldson and D. H. Waldren have described an outbreak in 1949 of three cases in Buckinghamshire (*Monthly Bulletin of the Ministry of Health*, February, 1951). Two of them were mild. The most severe was the foreman on the farm, who was admitted to hospital. He had lesions in all stages on his hands. Although his temperature was only 99° F. (37.2° C.) he was ill and looked toxaemic. His epitrochlear and axillary glands were enlarged. He had never been vaccinated. All the 18 cows were infected with cowpox.

Road Accidents in 1950

During 1950, reports the Ministry of Transport, 201,325 persons were killed or injured in 166,592 road accidents in Great Britain. This was the highest total of road casualties for any year since the war, and was 24,546 (14%) more than that for 1949.

Deaths numbered 5,012, an increase of 239 compared with the previous year, and were more than 5,000 for the first time since 1946. The seriously injured totalled 48,652, an increase of 5,242 over the 1949 figure. The position was adversely affected by the abolition of petrol rationing in May and the increase in the number of motor vehicles on the road. The best feature of the 1950 records is a reduction in the number of child deaths, the total of 868 being the lowest for more than 27 years.

The greatest proportionate increase in casualties was among motor-cyclists and their passengers, the total of 37,390 being 10,943 (41%) more than in 1949.

The following Table shows the figures of casualties for 1938, 1949, and 1950:

	Deaths	Seriously Injured	Slightly Injured
1938	6,648	50,782	175,929
1949	4,773	43,410	128,596
1950	5,012	48,652	147,661

Of the total number of road accidents, about 10% were attributed by the police primarily to the actions of motor-cyclists, 27% to drivers of other vehicles, 16% to pedal-cyclists, and 27% to pedestrians. The most prevalent factors in accidents attributed primarily to motor-cyclists were excessive speed, overtaking improperly, skidding, and misjudging distance, clearance, or speed; and in the case of other drivers, misjudgment, turning right without due care, careless crossing at road junctions, and overtaking improperly. Inattention and turning right without due care were the most common factors in accidents attributed primarily to the actions of pedal cyclists. In addition, 12,168 accidents, nearly 7½% of the total, occurred while passengers were either boarding or alighting from vehicles or through passengers falling inside the vehicles.

In December, 1950, there were 15,762 road casualties, including 366 killed and 3,769 seriously injured. Compared with December, 1949, there was a decrease of 751 in the total casualties and of 431 in the seriously injured. The decrease is probably due to the heavy snow which kept many people and much traffic off the roads. Child deaths numbered 39, which were 17 fewer than in December, 1949.

Week Ending February 24

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 828, whooping-cough 5,928, diphtheria 43, measles 27,776, acute pneumonia 1,656, acute poliomyelitis 21, dysentery 1,366, paratyphoid fever 13, typhoid fever 5. In the great towns 317 deaths were attributed to influenza.

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles for the week ending February 17 (No. 7).

Figures of notified *cases* are for: (*a*) England and Wales (London included). (*b*) London (administrative county). (*c*) Scotland. (*d*) Northern Ireland. (*e*) Eire. Figures of *births and deaths* and of *deaths* recorded under each disease are for: (*a*) The 126 great towns in England and Wales (London included). (*b*) London (administrative county). (*c*) The 16 principal towns in Scotland. (*d*) The 10 principal towns in Northern Ireland. (*e*) The 13 principal towns in Eire. A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, Northern Ireland, and Eire, the Ministry of Health and Local Government of Northern Ireland, and the Department of Health of Eire.

Disease	1951 Week Ending February 17					1950 Corresponding Week					1942–50 England & Wales Corresponding Week		
	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	Highest	Median	Lowest
Diphtheria	40	8	15	—	1	80	8	21	3	2	851	427	80
Deaths	—	—	—	—	—	1	—	—	—	—			
Dysentery	972	42	266	6	1	344	22	97	—	—	357	191	41
Deaths		—		—					—				
Encephalitis, acute	10	1	—	—		3	—	—	—	—	5	1	—
Deaths		—			—		—			—			
Erysipelas			25	6	6			31	4	12			
Food-poisoning	99	29		1		16	2		—				
Infective enteritis or diarrhoea under 2 years				13	10					13			
Deaths	21		3	1	4	25		3	—	6			
Measles*	24,585	3,178	219	52	67	4,526	71	77	347	137	19,502	7,209	1,487
Deaths		2	—	—	—			—	—	—			
Meningococcal infection	50	11	17	3	1	59	6	17	—	—	186	73	36
Deaths		1	1				1	1					
Ophthalmia neonatorum	24	3	7	—		24	2	8	—	—	88	74	24
Pneumonia, influenzal	2,115	107	33	25	93	1,189	78	64	13	—	1,469	1,206	788
Deaths (from influenza)†	492	52	14	11	50	76	8	18	—	3			
Pneumonia, primary			272					363					
Deaths	535	68		17	18	353	49		28	16			
Poliomyelitis, acute:													
Paralytic	18	—	3	—	—	39	3	—	1	5	39	8	1
Non-paralytic	6	1											
Deaths§	4	—			—	9	1			—			
Puerperal fever			6				—	4					
Puerperal pyrexia‖	67	9	5	4	1	80	9	6	3	—	182	147	80
Scarlet fever	904	68	159	25	52	2,130	134	233	148	89	2,130	1,497	1,051
Deaths		—	—	—	—			—	—	—			
Smallpox	1	—	—	—		—	—	—	—	—			
Deaths				—					—	—			
(1) Tuberculosis, respiratory			178	37				169	32				
(2) Tuberculosis, non-respiratory			22	3				31	6				
(1) Deaths	183	27	22	6	17	227	29	43	4	16			
(2) Deaths		3	6	1	6		7	4	3	3			
Typhoid fever	4	2	—	—	5	10	5	4	—	1	16	9	4
Deaths¶	—	—	—	—		—	—	—	—	—			
Paratyphoid fever	11	1	1 (B)	—		6	—	1 (B)	—	—			
Whooping-cough	5,662	404	778	52	97	1,652	68	401	52	103	3,027	1,652	1,209
Deaths	14	3	2	—	1	5	—	1	—	—			
Deaths (0–1 year)	301	39	33	6	18	331	44	48	13	32	579	401	331
Deaths (excluding stillbirths)	7,688	1,162	765	158	315	6,249	953	864	172	258	8,091	5,961	4,801
Annual death rate (per 1,000 persons living)			15·4					17·4					
Live births	7,104	1,208	905	242	361	7,720	1,223	941	210	507	10,195	7,567	5,654
Annual rate per 1,000 persons living			18·3					18·9					
Stillbirths	179	18	30			215	23	36			288	226	202
Rate per 1,000 total births (including stillborn)			32					37					

* Measles not notifiable in Scotland and returns are approximate. † Includes primary form for England and Wales, London, and N. Ireland. § The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, and London (administrative county), are combined. ‖ Includes puerperal fever for England and Wales and for Eire. ¶ Deaths from paratyphoid fever are combined with those from typhoid fever.

Medical News

Dinner to Sir William Kelsey Fry

A dinner organized by representatives of the various dental bodies was held at the Royal College of Surgeons of England in Lincoln's Inn Fields on Wednesday, February 21, to give the friends and colleagues of Sir William Kelsey Fry the opportunity of congratulating him on his recent knighthood. The Duke of Gloucester was among those present. The health of Sir William Kelsey Fry, with that of Lady Fry, was proposed by Mr. Arthur Bulleid, Air Commodore G. A. Ballantyne, and Mr. C. W. Roberts. After the dinner the President of the College, Sir Cecil Wakeley, who had been in the chair, presented Sir William with an album containing the signatures of all those present.

Supply of Doctors in the United States

There is likely to be a surplus of doctors in the United States in the 1960s, believes Dr. Frank Dickinson, economist and statistician of the American Medical Association. This is because progress in the practice of medicine has brought about an "increase in output" of at least one-third for each doctor, he told a Chicago meeting of the Federation of State Medical Boards, and because doctors cannot become "war-surplus" after the present emergency. Dr. Dickinson's opinions, which were personal, were in sharp contrast to those of other speakers at the meeting, who contended that training of doctors must be expanded or speeded up to avoid a shortage. Dr. Howard Rusk, chairman of the Health Resources Advisory Committee of the U.S. National Security Resources Board, estimated that the nation would have a deficit of 22,000 doctors in 1954, which would remain undiminished in 1960 unless there were expansion or acceleration, or both. He based his estimate on a U.S. military strength of 5,000,000 men continuing at that level until the end of 1960. If the Forces were not increased beyond 3,500,000 men the deficit in the number of doctors would be some 20,000, he predicted. Dr. Rusk was supported by Dr. Joseph Hinsey, of Cornell University Medical College, and Dr. Stockton Kimball, dean of the University of Buffalo Medical College, who told the meeting that medical schools had increased their intake during the past 10 years to an extent equal to the opening of 15 entirely new medical schools. There are 26,913 students in medical schools to-day, he said, or 1,090 more than last year and almost 5,000 more than 10 years ago.

Special Course on Rehabilitation of Children

A special eight-weeks course on the rehabilitation of physically handicapped children opened in London on March 5 under Governmental auspices. It is being financed jointly by W.H.O., U.N., and Unicef, and attended by teams from Austria, Finland, France, Germany, Greece, Italy, and Yugoslavia. Each team includes an orthopaedic surgeon, a physiotherapist or remedial gymnast, an occupational therapist, a teacher of crippled children, a social worker, a vocational training instructor, and a prosthetics technician. There are many thousands of European children crippled as the result of malnutrition or war injury, and Unicef is supplying equipment and apparatus to various Continental institutions for rehabilitation. The purpose of the present course is to make a start in teaching people how to use the new apparatus and practise modern methods.

Publications Received

West London Hospital Department of Rheumatic Diseases: *Annual Report, 1950.*

Society for the Study of Fertility. No. 1, Edinburgh Conference, 1949: *Proceedings.* 1950. (Heffer. Price 10s.)

National Smoke Abatement Society: *Proceedings of the Margate Conference, 1950.* (Price 6s.)

H.M.S.O.: *The Purification of the Water of Swimming-baths.* 1951.

National Corporation for the Care of Old People: *Third Annual Report, 1950.*

International Hospital Federation: *Report of Study Tour of Hospitals in Sweden.*

The Tavistock Clinic: *Report for 1949.*

Eugenics Society: *Statement of Objects.* 1950.

Wills

Dr. John Francis Kirwan, late senior ship surgeon of the Union Castle Line, left £2,769. Dr. Ernest Douglas Wolff, formerly for many years in practice at Foulsham, left £13,284. Dr. William Gillon Brand, formerly for over 40 years in practice in Adlington, near Chorley, Lancs, and who established Springfield Farm, Adlington, left £16,806. Dr. Alfred William Moore, late Deputy Director-General of the Ministry of Pensions, left £20,051. Dr. John Forbes Ward, of Manchester, a governor of Stockport Grammar School, left £47,778. Rev. Charles Anderson Meaden, of The Presbytery, Thetford, Norfolk, left £2,967, including £100 to be distributed to poor missions for Masses. Dr. James Henry Ferguson, formerly for many years in practice in Keighley, Yorkshire, left £19,997. Dr. William Patrick McGrenahan, a general practitioner in Wolverhampton, left £20,415, including £500 to the parish priest of SS. Mary and John's Catholic Church, Wolverhampton, for charitable purposes in his parish. Dr. Ernest Thomas Jensen, part founder of the Institute for the Scientific Treatment of Delinquency, left £17,250. After bequests and legacies totalling £675 he left one-third of the residue for charities or charitable institutions at the discretion of his trustees.

COMING EVENTS

Oxford and Cambridge Boat Race

Messrs. Vitamins Limited announce that they have available a limited number of tickets for doctors who may wish to view the Boat Race from their premises. Early applications should be made to Dept. B.R.2, Vitamins Limited, Upper Mall, London, W.6.

Second International Gerontological Congress

Held at the Hotel Jefferson, St. Louis, Missouri, September 9–14, this will be under the sponsorship of the International Association of Gerontological Societies, the Gerontological Society, Inc., and the American Geriatrics Society.

Section I of the programme—Biology and Medicine—is directed by John Esben Kirk, Department of Gerontology, Washington University Medical School, 5600, Arsenal Street, St. Louis 9, Mo. Section II—Sociology, Psychology, Education, and Religion—Dr. Robert J. Havighurst, Committee on Human Development, University of Chicago, Chicago 37, Ill. Section III—Economics and Welfare—Professor Edwin E. Witte, Department of Economics, University of Wisconsin, Madison, Wis. Section IV—Medical Services, Hygiene, and Housing—Dr. Joseph W. Mountin, Associate Chief, Bureau Medical Services, U.S. Public Health Service, Washington, D.C. Programme directors are assisted by advisors.

Communications concerning papers should be sent to the director concerned. The general plan is to have many short papers, several symposia, and sessions devoted to problem identification in each division. Dr. Albert I. Lansing, Department of Anatomy, Washington University Medical School, 660, South Kingshighway, St. Louis 10, Mo., is the chairman of the committee on exhibits. Titles of papers with abstracts of not more than 200 words must be received by the programme directors before May 1 and descriptive summaries of exhibits by Dr. Lansing, also before May 1. The registration fee is $10. It is recommended that room reservations be made as soon as possible at the Jefferson Hotel, St. Louis 3, Mo.

Short Course on "The Epileptic"

A one-day course is being held at the Victoria Hall, Bloomsbury Square, London, W.C.1, on Thursday, March 15, from 10 a.m. to 5 p.m. In the morning there will be papers on social aspects of epilepsy, including delinquency; and in the afternoon the training and employment of epileptics will be discussed. Further information from the general secretary, British Council for Rehabilitation, Tavistock House (South), Tavistock Square, W.C.1.

The Osler Club of London

The next meeting will be held on Friday, March 30, at 7.45 p.m. at 11, Chandos Street, London, W.1. Dr. Hugh Sinclair, director, Laboratory of Human Nutrition, University of Oxford, will read a paper on "The History of Nutrition." The discussion will be opened by Professor V. H. Mottram and Dr. A. L. Bacharach.

Joseph Clover Lecture

Dr. R. J. Minnitt will deliver the Joseph Clover Lecture on "Some Factors Reviewed which Influence the Reassessment of Ether as an Anaesthetic Agent" before the Faculty of Anaesthetists at the Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C., on Wednesday, March 14, at 5 p.m.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Sunday

INTERNATIONAL HAEMOPHILIA SOCIETY.—At Society for Visiting Scientists, 5, Old Burlington Street, London, W., Sunday, March 11, 2.30 p.m., annual general meeting.

Monday

●INSTITUTE OF CHILD HEALTH, Hospital for Sick Children, Great Ormond Street, London, W.C.—March 12, 5 p.m., *"The Control of Inheritable Defects,"* by Dr. J. A. Fraser Roberts.

INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, London, W.C.—March 12, 5 p.m., *"Cerebellar Mechanisms,"* by Professor F. Bremer (Brussels).

INSTITUTE OF OPHTHALMOLOGY, Judd Street, London, W.C.—March 12, 5.30 p.m., *"Antihistamine Drugs in Ophthalmology,"* by Mr. A. G. Cross.

MEDICAL SOCIETY OF LONDON, 11, Chandos Street, Cavendish Square, W.—March 12, 8.30 p.m., discussion: *"Nature and Treatment of Fibrositis,"* to be introduced by Drs. A. H. Douthwaite and C. B. Heald.

SOCIETY OF PUBLIC ANALYSTS: BIOLOGICAL METHODS GROUP.—At Chemical Society's Room, Burlington House, Piccadilly, London, W., March 12, 6.30 p.m., discussion, *"The Evaluation of Drugs in Man."* Papers: *"The Evaluation of Drugs in Man, With Special Reference to Antihistaminics,"* by Professor W. A. Bain; *"Tests on Analgesic Drugs in Man,"* by Dr. C. A. Keele.

Tuesday

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C., March 13, 5.30 p.m., *"Statistics in Medical Research,"* by Professor A. Bradford Hill, Ph.D., D.Sc.

CHADWICK TRUST.—At Royal Sanitary Institute, 90, Buckingham Palace Road, London, S.W., March 13, 2.30 p.m., *"Insect Infestation of Stored Foodstuffs,"* Chadwick Public Lecture by Mr. G. V. B. Herford.

CHELSEA CLINICAL SOCIETY.—At South Kensington Hotel, 47, Queen's Gate Terrace, London, S.W., March 13, 7 for 7.30 p.m., discussion: *"Some Literary Diagnoses,"* to be opened by Dr. Russell Brain, P.R.C.P., followed by Mr. Edward Shanks and Mr. Lionel Hale.

EUGENICS SOCIETY.—At Royal Society, Burlington House, Piccadilly, London, W., March 13, 5.30 p.m., *"A Study of Neuroticism in Twins,"* by H. J. Eysenck, D.Sc., Ph.D.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—March 13, 5 p.m., *"Lipoid Affections of the Skin,"* by Dr. I. Muende.

INSTITUTE OF PHYSICS: ELECTRONICS GROUP, 47, Belgrave Square, London, S.W.—March 13, 5.30 p.m. (approx.), *"Plasma Oscillations,"* by Dr. D. Gabor, F.Inst.P.

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, London, S.W.—March 13, 5 p.m., *"Aspects of the Circulation's Economy,"* Oliver-Sharpey Lecture by Professor K. J. Franklin. (See also March 15.)

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—March 13, 5 p.m., *"Functional Results following Sphincter-saving Excisions of the Rectum,"* Hunterian Lecture by Dr. J. C. Goligher.

Wednesday

FACULTY OF ANAESTHETISTS, Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.—March 14, 5 p.m., *"Some Factors Reviewed Which Influence the Reassessment of Ether as an Anaesthetic Agent,"* Joseph Clover Lecture by Dr. R. J. Minnitt.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—March 14, 5 p.m., *"X-ray Technique,"* by Dr. C. W. McKenny.

LONDON COUNTY MEDICAL SOCIETY.—At Colindale Hospital, The Hyde, Hendon, N.W., March 14, 3 p.m., clinical meeting.

NORTH-EAST LONDON CLINICAL SOCIETY.—At Prince of Wales's General Hospital, Tottenham, N., March 14, 8 p.m., *"The Surgery of Deafness—Fenestration Operation,"* by Mr. W. S. McKenzie. Demonstration cases will be shown.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—March 14 (1) 3.45 p.m., *"Tumours of the Breast,"* Erasmus Wilson Demonstration by Mr. C. E. Shattock; (2) 5 p.m., *"Some Factors Reviewed which Influence the Reassessment of Ether as an Anaesthetic Agent,"* Joseph Clover lecture by Dr. R. J. Minnitt.

●ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, London, W.—March 14, 3.30 p.m., *"The Heating and Ventilation of Houses,"* by Mr. G. D. Nash.

ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh.—March 14, 8 p.m., annual extraordinary general meeting.

ROYAL SANITARY INSTITUTE, 90, Buckingham Palace Road, London, S.W.—March 14, 2.30 p.m., discussion: *"The Day Care of Children apart from their Parents,"* to be opened by Dr. Hugh Paul, Gertrude Willoughby, M.A., and Dr. Hilda Menzies.

Thursday

BRITISH INSTITUTE OF RADIOLOGY, 32, Welbeck Street, London, W.—March 15, 8.15 p.m., *"Some Impressions of Radiobiological Progress in the United States,"* by Dr. L. F. Lamerton.

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C., March 15, 5.30 p.m., *"Application of Radioactive Isotopes to Medical Research Problems,"* by Dr. E. E. Pochin.

EDINBURGH CLINICAL CLUB.—At B.M.A. Rooms, 7, Drumsheugh Gardens, Edinburgh, March 15, 8 p.m., *"Functional Dyspepsia,"* by Dr. G. J. Alexander.

HARVEIAN SOCIETY OF LONDON.—At Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C., March 15, 8.15 p.m., *"The Surgery of the Spleen,"* Harveian Lecture by Sir James Learmonth.

INSTITUTE OF OPHTHALMOLOGY, Judd Street, London, W.C.—March 15, 5.30 p.m., *"Structural Biochemistry of Eye Tissues,"* by Mr. A. Pirie.

LIVERPOOL MEDICAL INSTITUTION.—At Royal Infirmary, Chester, March 15, 3.30 p.m., joint meeting with Chester and North Wales Medical Society. Afternoon clinical demonstration.

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, London, S.W.—March 15, 5 p.m., *"Aspects of the Circulation's Economy,"* Oliver-Sharpey Lecture by Professor K. J. Franklin. (See also March 13).

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—At Royal Army Medical College, Millbank, London, S.W., March 15, 7.30 p.m., laboratory meeting. Various demonstrations will be given.

ST. ANDREWS UNIVERSITY.—At Lecture Theatre, Materia Medica Department, Medical School, Small's Wynd, Dundee, March 15, 5 p.m., the Final Lecture by Sir Andrew Davidson.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—March 15, 4.30 p.m., lecture-demonstration on neurology.

Friday

BIOCHEMICAL SOCIETY.—At Department of Biochemistry, University College, London, W.C., March 16, 11.30 a.m., annual general meeting; 2 p.m., scientific papers will be read.

FACULTY OF RADIOLOGISTS.—At Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C., March 16, 2.15 p.m., Therapy Section Meeting. Discussion: *"Primary Tumours Involving the Spinal Cord,"* speakers, Professor T. Crawford, Dr. J. W. D. Bull, Mr. Wylie McKissock, and Dr. J. Jackson Richmond.

INSTITUTE OF OPHTHALMOLOGY, Judd Street, London, W.C.—March 16, 5.30 p.m., *"Optic Nerve Compression,"* by Dr. S. P. Meadows.

INSTITUTE OF PHYSICS: INDUSTRIAL RADIOLOGY GROUP, 47, Belgrave Square, London, S.W.—March 16, 6.30 p.m., "*The Physics of Radiography*," by Mr. H. S. Peiser, A.Inst.P.

●ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—At St. George's Hospital (Board Room), Hyde Park Corner, London, S.W., March 16, 5.30 p.m., "*Jenner's Cowpox Inoculation*," Jenner Memorial Lecture by Professor A. W. Downie.

SOCIETY OF PUBLIC ANALYSTS.—(1) At Royal Society, Burlington House, Piccadilly, London, W., March 16, 3.15 p.m., annual general meeting. Address of Retiring President, Mr. George Taylor. (2) At Society of Apothecaries of London, Blackfriars Lane, London, E.C., March 16, 7 for 7.30 p.m., Biennial Dinner.

APPOINTMENTS

CRAWFORD, JAMES MACKAY, M.D., D.P.M., Consultant Psychiatrist and Physician-Superintendent, Botleys Park Hospital, Chertsey, Surrey.

CROWLEY, NORA VERONICA, M.B., B.Ch., D C H., Assistant Medical Officer for Maternity and Child Welfare and School Medical Inspection Northamptonshire County Council.

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—The following appointments are announced: C. H. Budd, B.M., B.Ch., F F.A., Part-time Consultant Anaesthetist, Saffron Walden General Hospital; E. L. Dutta, M.R.C.S., L.R.C.P., Resident Medical Officer, County Hospital. Doddington, Cambridgeshire; G. E. Flatman, M.B., B.S., Resident Surgical Officer, West Norfolk and King's Lynn Hospital; C. I. Cooling, M B., B S., Junior Resident Surgical Officer, East Suffolk and Ipswich Hospital and Ipswich Borough General Hospital.

EGERTON, B. H., M.B., B.S., Anaesthetic Registrar, Norfolk and Norwich Hospital, East Anglian Regional Hospital Board.

EVANS, W. E. F., M R.C.S., L.R.C.P., D.A., Consultant Anaesthetist and Medical Director, Ashford Hospital, Middlesex.

HURLEY, JEREMIAH, M.Ch., F.R.C.S.Ed., Senior Surgeon, Meath Hospital, Dublin.

KILLOH, R. BRUCE, M.B., Ch.B., D.P.H., Medical Officer of Health, Melksham Urban and Bradford and Melksham Rural Districts, Wilts.

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—*Consultant Ophthalmic Surgeon at Southmead Hospital, Bristol*, P. Jardine, F.R.C.S.Ed., D.O.M.S. *Consultant Orthopaedic Surgeons in Bristol Clinical Area*, H. K. Lucas, M.Ch Orth., F.R.C.S.Ed., M. P. McCormack, F.R.C.S Ed. *Deputy Resident Physician, Ham Green Hospital, Bristol*, G. D. W. McKendrick, B.M., B.Ch., M.R.C.P. *Senior Registrar in Plastic Surgery, Frenchay Hospital, Bristol*, G. S. Gunter, M.S., F.R.C.S., F.R.A.C.S.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Borrie.—On March 4, 1951, at Newcastle-upon-Tyne, to Helen, wife of John Borrie, M.B.E., F.R.C.S., a son—Michael John.

Crawford.—On February 21, 1951, at the Edgbaston Maternity Nursing Home, Birmingham, to Mary Stewart, wife of Dr. W. Cowan Crawford, a daughter—Fiona Mary.

Hutton.—On March 2, 1951, at the Leeds Maternity Hospital, to Dorothy (formerly Cheshire), wife of Mr. Thomas B. Hutton, M.B., F.R.C.S.Ed., a sister for David and Christopher—Ann Dorothy Elizabeth.

Starks.—On February 23, 1951, to Dr. Isobel Starks (formerly Morrison), wife of Dr. J. M. Starks, of High Street, Wembourn, Staffs, a son.

DEATHS

Alton.—On March 2, 1951, at Rookery Dene, 1,856, Pershore Road, King's Norton, Birmingham, Edgar Hepworth Alton, L.R.C.P.&S.Ed., L.R.F.P.S., aged 81.

Anderson.—On February 16, 1951, at Seascale, Cumberland, Charles Madill Anderson, M.B., Ch.B., late of Sheffield, aged 75.

Arbuckle.—On February 17, 1951, at Durban, South Africa, Mary Scott Arbuckle (formerly Anderson), M.B., Ch.B.

Bradley.—On February 27, 1951, at 1a, Watling Street Road, Fulwood, Preston, Lancs, David Kelly Bradley, M.B., Ch.B.

Browne.—On February 27, 1951, at Rapallo, Italy, Cuthbert Garrard Browne, C.M.G., D.S.O., M.R.C.S., L.R.C.P., Lieutenant-Colonel, R.A.M.C., retired, of Lakers Farm, West Ch llington, Sussex.

Davies.—On March 5, 1951, at a Manchester nursing-home, Evan Sherrah Davies, M.R.C.S., L.R.C.P., of Gaghills House, Waterfoot, Rossendale.

Dykes.—On February 24, 1951, at Hove, David Garfield Dykes, M.B., Ch.B., formerly of Great Witley and Kidderminster, Worcs, aged 69.

Eddlestone.—On February 16, 1951, Neville Avory Eddlestone, M.D., of 70, Marine Avenue, Monkseaton, Northumberland, aged 66.

Falconar.—On March 2, 1951, William Ernest Falconar, M.B., of Picton Cottage, Twyford, Berks, aged 79.

Maunder.—On March 3, 1951, at Erith, Harold Arthur Maunder, D.S.O., M.B., B.S., of Ormiston, 68, Bexley Road, Erith, Kent.

Molesworth.—On February 27, 1951, at Cruicksfield, Duns, Berwicks, William Molesworth, C.I.E., C.B.E., M.B., B.S., Colonel, I.M.S., retired, aged 85.

Montgomery.—On March 4, 1951, at St. Richard's Hospital, Chichester, Edwin Cecil Montgomery, M.R.C.S., L.R.C.P., of 32, Crescenta Walk, Bognor Regis, late of Maidenhead, aged 79.

Shaw.—On February 27, 1951, Kenneth Rodas Devaignes Shaw, L.R.C.P.& S.Ed., L.R.F.P.S., of 7, Harley Street, London, W.

Williams.—On February 25, 1951, at Milford House, Milford Haven, Pemb., Hugh Owen Williams, M.B., B.S., D.P.H., of Abersoch.

Williamson.—On February 23, 1951, at Grimsby General Hospital, Joshua Williamson, M.B., Ch.B., of 14, Lindum Road, Cleethorpes, Lincs.

Young.—On March 2, 1951, at Burnbank House, Kilsyth, near Glasgow, Watson Young, M.B., Ch.B., aged 71.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Coronary Thrombosis

Q.—*What is the first-aid and immediate medical treatment of a patient suspected of having sustained a coronary thrombosis?*

A.—First-aid treatment usually consists in persuading the patient to sit quietly in a chair with his legs down, withholding all food, fluid (including alcohol), and stimulants, and giving a large dose of any analgesic that is handy, such as aspirin (15 to 20 gr.—1 to 1.3 g.). If there is much dyspnoea, venous tourniquets may be placed round the thighs. If there is syncope or faintness, the patient should be made to lie down with his head low, and venous tourniquets must not be applied.

Immediate medical treatment includes the giving of ¼ gr. (22 mg.) of morphine, and perhaps heparin 10,000 units intravenously. If the patient is known to be sensitive to morphine, 50–100 mg. of pethidine may be injected intramuscularly instead. Oxygen may help in some cases, but is not used routinely in this country. Aminophylline and papaverine also have their advocates. Quinidine (3 to 6 gr.—0.2 to 0.4 g.) three times a day helps to prevent paroxysmal changes in rhythm.

The patient should be nursed in bed, flat if shocked or faint, propped up if dyspnoeic. Semi-starvation for the first 48 hours is important, fruit drinks with sugar, tea with milk and sugar, and perhaps a little stewed or tinned fruit with milk and rice being all that are allowed. An enema may be given on the fourth or fifth day if necessary, but not before.

Aeroplane Dope

Q.—*What is the composition of aeroplane dope? To what toxic symptoms may it give rise, and what is the treatment in such cases?*

A.—The term "aeroplane dope" survives from the 1914–18 war, when cellulose acetate was dissolved in tetrachlorethane to make a waterproof coating for aeroplane wings. Seventy cases of toxic jaundice, with 12 deaths, had occurred up to 1917 among workers exposed to this substance, and the workers themselves called it "dope" because it made them ill. Attempts to solve the problem by reducing the quantity of tetrachlorethane in the dope failed, for even as little as 10% proved dangerous (Hunter, 1944). In July, 1917, the War Office and the Admiralty were able to announce that no dope containing tetrachlorethane was being made or used.

In the 1939–45 war, coal-tar benzene was used as a solvent in aeroplane dope. The amount of benzene depended upon the availability of other solvents such as xylene and toluene, but did not exceed 15%. Modern formulations have not altered greatly. The risk of poisoning depends upon the exposure to benzene. Toluene and the higher homologues of benzene have no long-term toxic action, but commercial toluol and xylol may contain benzene as an impurity.

Acute poisoning is not likely to occur in workers engaged on aeroplane "doping." Chronic benzene poisoning may occur, and no satisfactory method has been devised to detect it in its earliest stage. Repeated exposure to benzene may cause severe and often fatal anaemia from its toxic effect upon the bone marrow. Early workers considered that a diagnosis of benzene poisoning was not justified unless there was an aplastic anaemia associated with granulocytopenia.

It is now known that anaemias caused by benzene may be macrocytic or microcytic, and the different components of the blood may be affected in varying degree.

Hunter, Milton, Perry, Barrie, Loutit, and Marshall (1944) reported an investigation in 16 factories involving nearly 1,200 workers exposed to concentrations of benzene vapour varying between 5 and 15%. No significant changes in the blood were detected. The concentration of benzene in the atmosphere of the general workshop rarely exceeded 10 parts per million, and even on such specialized jobs as spraying the insides of cockpits the concentration did not rise above 45 parts per million, and then only for short periods of time. The toxic level for benzene in the atmosphere is usually stated to be 100 parts per million. Since some persons are unusually susceptible to its effects the only level which can be regarded as safe is zero.

Poisoning by benzene could be prevented by abandoning its use as a solvent. Where it is used, adequate ventilation must be achieved, and the odour of benzene in the workshop should be regarded as a danger signal. The development of light metals and alloys for use in aircraft construction has enabled "doping" of aircraft to be reduced to a minimum.

Treatment of chronic poisoning is by repeated blood transfusions. Recovery sometimes occurs even in seriously affected persons. No one who has had symptoms and signs of chronic poisoning should return to work involving further exposure to benzene.

REFERENCES

Hunter, D. (1944). *Industrial Toxicology*, p. 64. Oxford.
—— Milton, R., Perry, K. M. A., Barrie, H. J., Loutit, J. F., and Marshall, T. S. (1944). *Brit. J. industr. Med.*, **1**, 237.

Morphine in Rheumatic Carditis in Children

Q.—*Are there any contraindications to the use of morphine as a sedative for a child with severe rheumatic carditis?*

A.—Morphine may be given to children with rheumatic pericarditis if pain and restlessness are considerable. It may occasionally be required in the restless child with congestive heart failure resulting from rheumatic heart disease. Apart from these two conditions it is not required in juvenile rheumatism, and in fact is definitely contraindicated; salicylates will rapidly control pain and restlessness in acute rheumatism, and barbiturates or paraldehyde are of more value in the restlessness of severe chorea.

Teaching Sphincter Control

Q.—*How may a child be taught control of his sphincters?*

A.—A child is certainly not trained by being potted after meals from early infancy. By this means a child may be conditioned to pass urine and faeces when placed on the pot, but this is an involuntary process, and such conditioning more often than not breaks down before voluntary sphincter control appears, usually at about 15 to 18 months. Apart from this conditioning it is probably impossible to "train" a child to acquire sphincter control.

At 15 to 18 months a child begins to indicate his desire to pass urine, and he can be helped by being placed on the pot immediately he shows signs of this and at other times when his bladder is likely to be full (e.g., when he comes in from outside on a cold day). Punishments for mishaps are likely to do nothing but retard sphincter control.

Later there comes a time, determined by the reliability with which the child indicates his wants, when he should be given the responsibility of doing without his napkin during the day; later still, of going and sitting on the pot without being placed there (this is usually possible between 2½ and 3 years of age). When it is clear that he is ready to do without a napkin at night, a pot is placed at his bedside for his use. It is doubtful whether any other sort of training does anything to help a child to acquire control, but unwise training will certainly delay its acquisition.

Berger–Kahn Test for Syphilis

Q.—*I am working in a bush hospital in the Tropics, where the nearest well-equipped laboratory is about 300 miles away. I am interested in the Berger–Kahn test for syphilis, and would be grateful for the following information: (1) How does the test compare in accuracy to the Wassermann and Kahn tests? (2) How should the stock serum be prepared, and how long can it be kept in a refrigerator? Is it best to employ "standard" Kahn antigen, or "sensitized" Kahn antigen? (3) How should the test be carried out? (4) How soon does the patient's serum give a positive reaction after infection? (5) Is there any way of distinguishing a positive reaction due to syphilis from one due to yaws, which is very prevalent in this area? (6) Is there any danger of "false positive" reactions due to leprosy, malaria, or other infections?*

A.—(1) The Berger–Kahn test is over-sensitive and less specific than the Wassermann or Kahn tests.

(2) The stock antigen, which keeps for at least a year at room temperature, is prepared as follows: To 10 parts of standard Kahn antigen containing 0.6% cholesterol and having a titre of 1+1.2 add 1 part of tinct. benz. co. *B.P.* To 10 ml. of this mixture add 17 mg. of Victoria blue 4R (Gurr). The container must be well stoppered.

(3) The latest description of the test can be obtained from the *British Medical Journal* (1947, **2**, 131).

(4) The patient's serum usually gives a positive result four to five weeks after infection. This, of course, is an average result, and it may take very much longer.

(5) Since the basic reacting constituent of the antigen is Kahn standard antigen it is reasonable to assume that there is no way of distinguishing a positive reaction due to syphilis from one due to yaws.

(6) For the same reason as in (5) the danger of false positive reactions due to leprosy, malaria, and other causes is very real.

Finally, it must be said that the performance of serum tests for syphilis in small hospitals by any but well-trained staff doing large numbers of tests regularly is not to be recommended.

Reactions to Penicillin

Q.—*What are the sensitivity or other reactions which are known to occur after intramuscular injections of penicillin?*

A.—It is presumed that the question refers to specific reactions to the drug itself, and not to such possible effects as infection at the site of injection or inflammatory reactions due to the material in which it is dispensed. The former occur only in sensitized subjects, and the usual manifestations are fever and urticaria; occasionally a condition resembling shock may follow an injection almost immediately. Other effects, involving organs such as kidney and bone marrow, have been reported so rarely that it may be doubtful whether they were in fact due to penicillin at all.

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